

Supporting information

Development of potent cholinesterase inhibitors based on a marine pharmacophore

Vijayaragavan Elumalai¹, Tomaž Trobec², Maja Grundner³, Christophe Labriere,¹ Robert Frangež², Kristina Sepčič³, Jørn H. Hansen¹ and Johan Svenson^{4,}*

¹Department of Chemistry, Chemical Synthesis and Analysis Group, UiT The Arctic University of Norway, N-9037, Tromsø, Norway.

²Institute of Preclinical Sciences, Veterinary Faculty, University of Ljubljana, 1000 Ljubljana, Slovenia

³Department of Biology, Biotechnical Faculty, University of Ljubljana, 1000 Ljubljana, Slovenia

⁴Cawthron Institute, 98 Halifax Street East, Nelson 7010, New Zealand

*Correspondence and requests for materials should be addressed to J.S. (Ph: +64 27 272 1876, email: Johan.svenson@cawthron.co.nz); orchid: 0000-0002-4729-9359

List of Contents:

- Figure S1.** ^1H -NMR and ^{13}C -NMR spectrum of **3** in DMSO
- Figure S2.** ^1H -NMR and ^{13}C -NMR spectrum of **4** in Methanol- d_4
- Figure S3.** ^1H -NMR and ^{13}C -NMR spectrum of **6d** in CDCl_3
- Figure S4.** ^1H -NMR and ^{13}C -NMR spectrum of **7** in CDCl_3
- Figure S5.** ^1H -NMR and ^{13}C -NMR spectrum of **8a** in Methanol- d_4
- Figure S6.** COSY and HSQC spectrum of **8a** in Methanol- d_4
- Figure S7.** HMBC spectrum of **8a** in Methanol- d_4
- Figure S8.** ^1H -NMR and ^{13}C -NMR spectrum of **8b** in Methanol- d_4
- Figure S9.** ^1H -NMR and ^{13}C -NMR spectrum of **8c** in Methanol- d_4
- Figure S10.** ^1H -NMR and ^{13}C -NMR spectrum of **8d** in Methanol- d_4
- Figure S11.** ^1H -NMR and ^{13}C -NMR spectrum of **8e** in Methanol- d_4
- Figure S12.** ^1H -NMR and ^{13}C -NMR spectrum of **9a intermediate** in Methanol- d_4
- Figure S13.** ^1H -NMR and ^{13}C -NMR spectrum of **9a** in Methanol- d_4
- Figure S14.** ^1H -NMR and ^{13}C -NMR spectrum of **9b intermediate** in Methanol- d_4
- Figure S15.** ^1H -NMR and ^{13}C -NMR spectrum of **9b** in Methanol- d_4
- Figure S16.** ^1H -NMR and ^{13}C -NMR spectrum of **9c intermediate** in Methanol- d_4
- Figure S17.** ^1H -NMR and ^{13}C -NMR spectrum of **9c** in Methanol- d_4
- Figure S18.** COSY and HSQC spectrum of **9c** in Methanol- d_4
- Figure S19.** HMBC spectrum of **9c** in Methanol- d_4
- Figure S20.** ^1H -NMR spectrum of **9d intermediate** in Methanol- d_4
- Figure S21.** ^1H -NMR and ^{13}C -NMR spectrum of **9d** in Methanol- d_4
- Figure S22.** ^1H -NMR and ^{13}C -NMR spectrum of **9e** in Methanol- d_4
- Figure S23.** ^1H -NMR and ^{13}C -NMR spectrum of **10a** in Methanol- d_4
- Figure S24.** COSY and HSQC spectrum of **10a** in Methanol- d_4
- Figure S25.** HMBC spectrum of **10a** in Methanol- d_4
- Figure S26.** ^1H -NMR and ^{13}C -NMR spectrum of **10b intermediate** in Methanol- d_4
- Figure S27.** ^1H -NMR and ^{13}C -NMR spectrum of **10b** in Methanol- d_4
- Figure S28.** ^1H -NMR and ^{13}C -NMR spectrum of **10c intermediate** in Methanol- d_4
- Figure S29.** ^1H -NMR and ^{13}C -NMR spectrum of **10c** in Methanol- d_4
- Figure S30.** ^1H -NMR and ^{13}C -NMR spectrum of **10d intermediate** in Methanol- d_4
- Figure S31.** ^1H -NMR and ^{13}C -NMR spectrum of **10d** in Methanol- d_4

Figure S1. ^1H -NMR and ^{13}C -NMR spectrum of **3** in DMSO

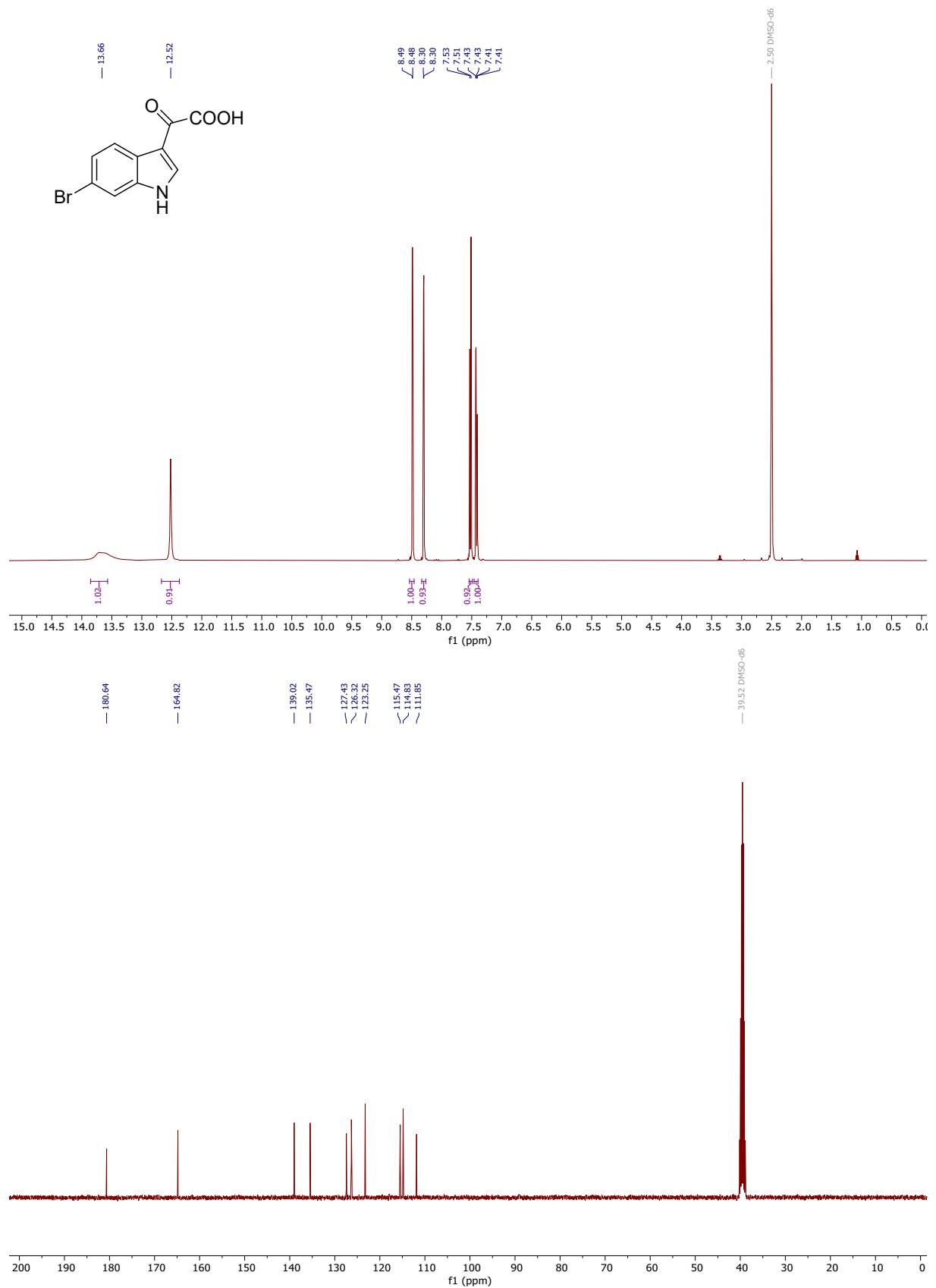


Figure S2. ^1H -NMR and ^{13}C -NMR spectrum of **4** in Methanol- d_4

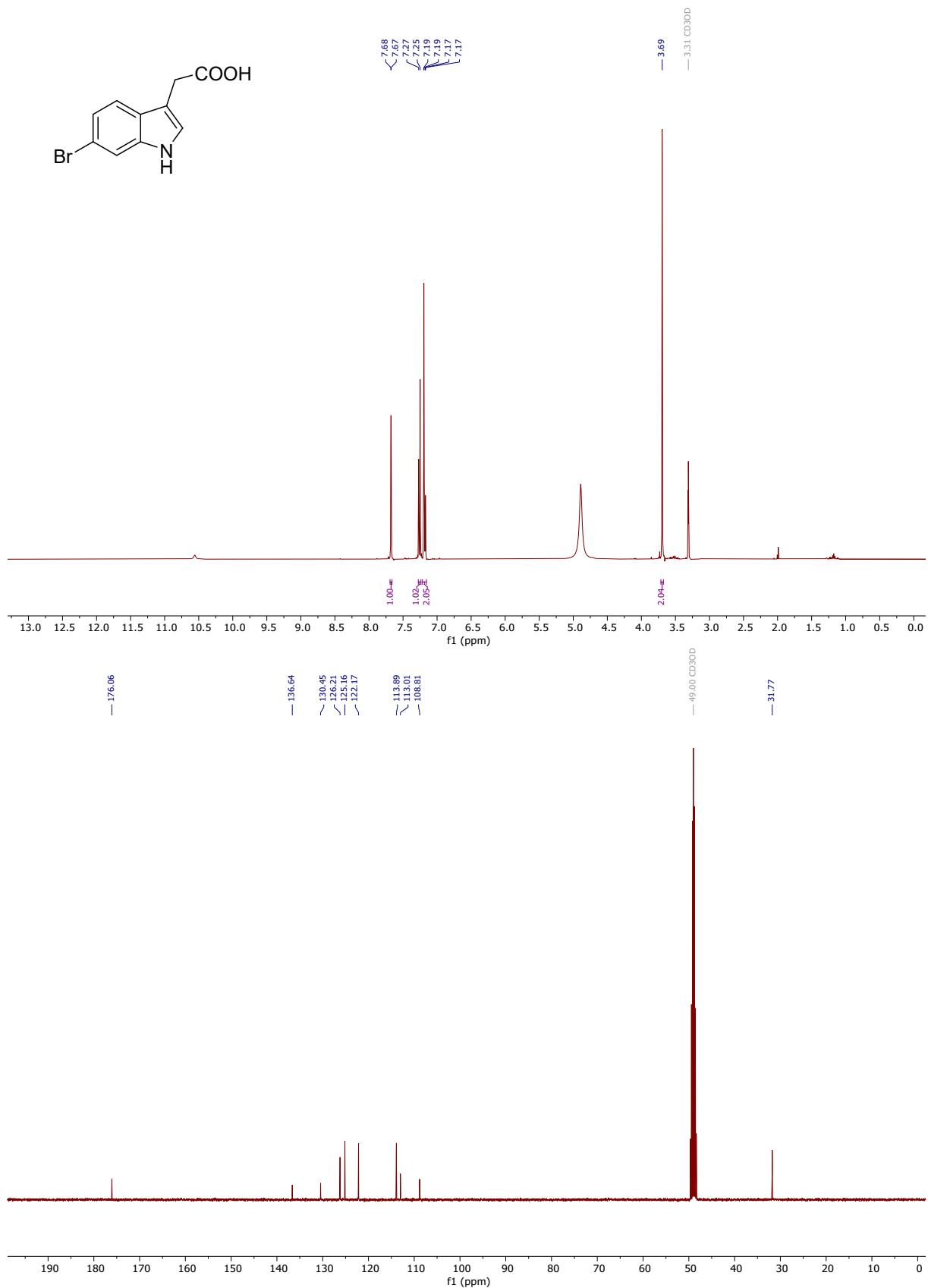


Figure S3. ^1H -NMR and ^{13}C -NMR spectrum of **6d** in CDCl_3

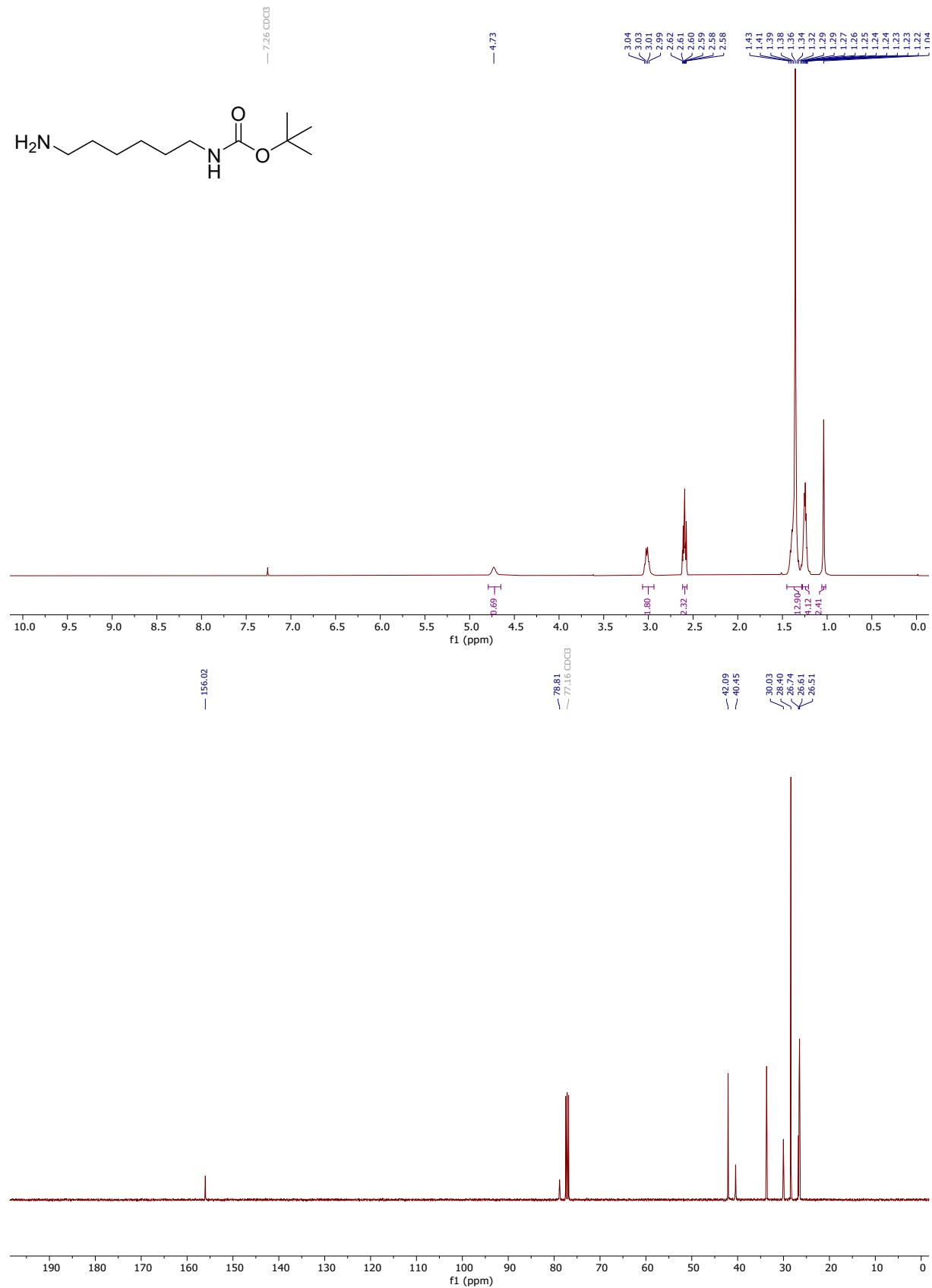


Figure S4. ^1H -NMR and ^{13}C -NMR spectrum of **7** in CDCl_3

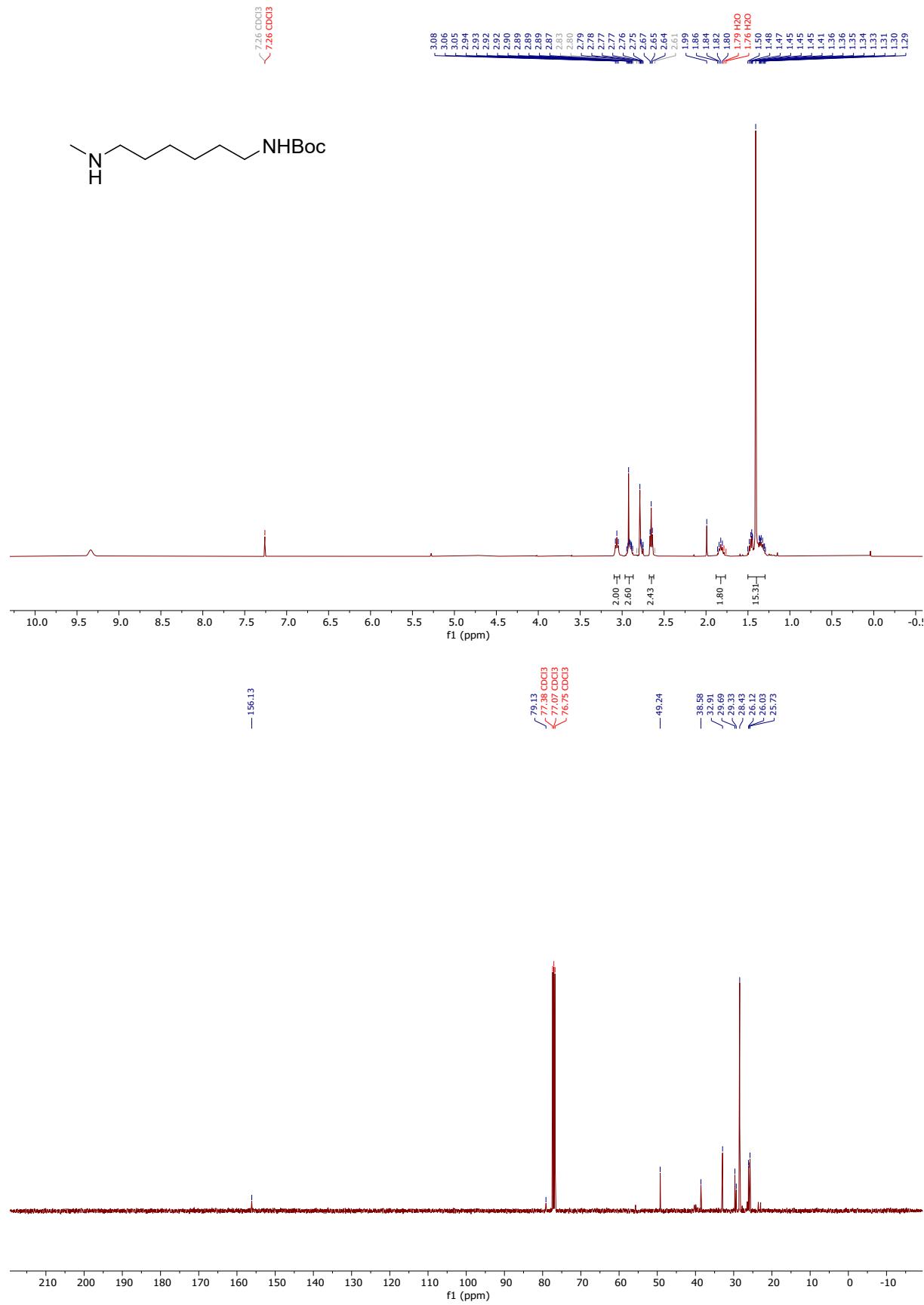


Figure S5. ^1H -NMR and ^{13}C -NMR spectrum of **8a** in Methanol- d_4

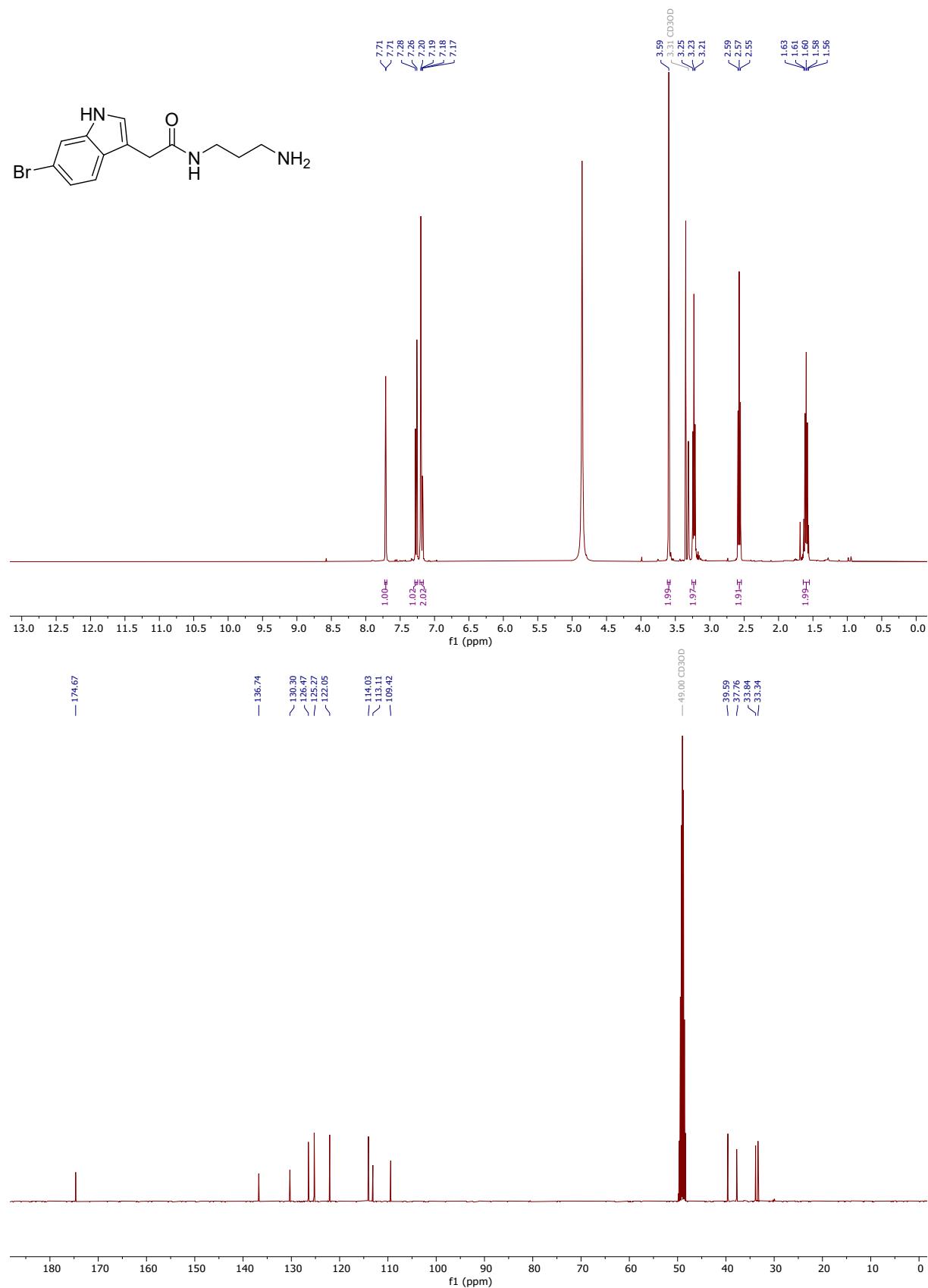


Figure S6. COSY and HSQC spectrum of **8a** in Methanol-*d*₄

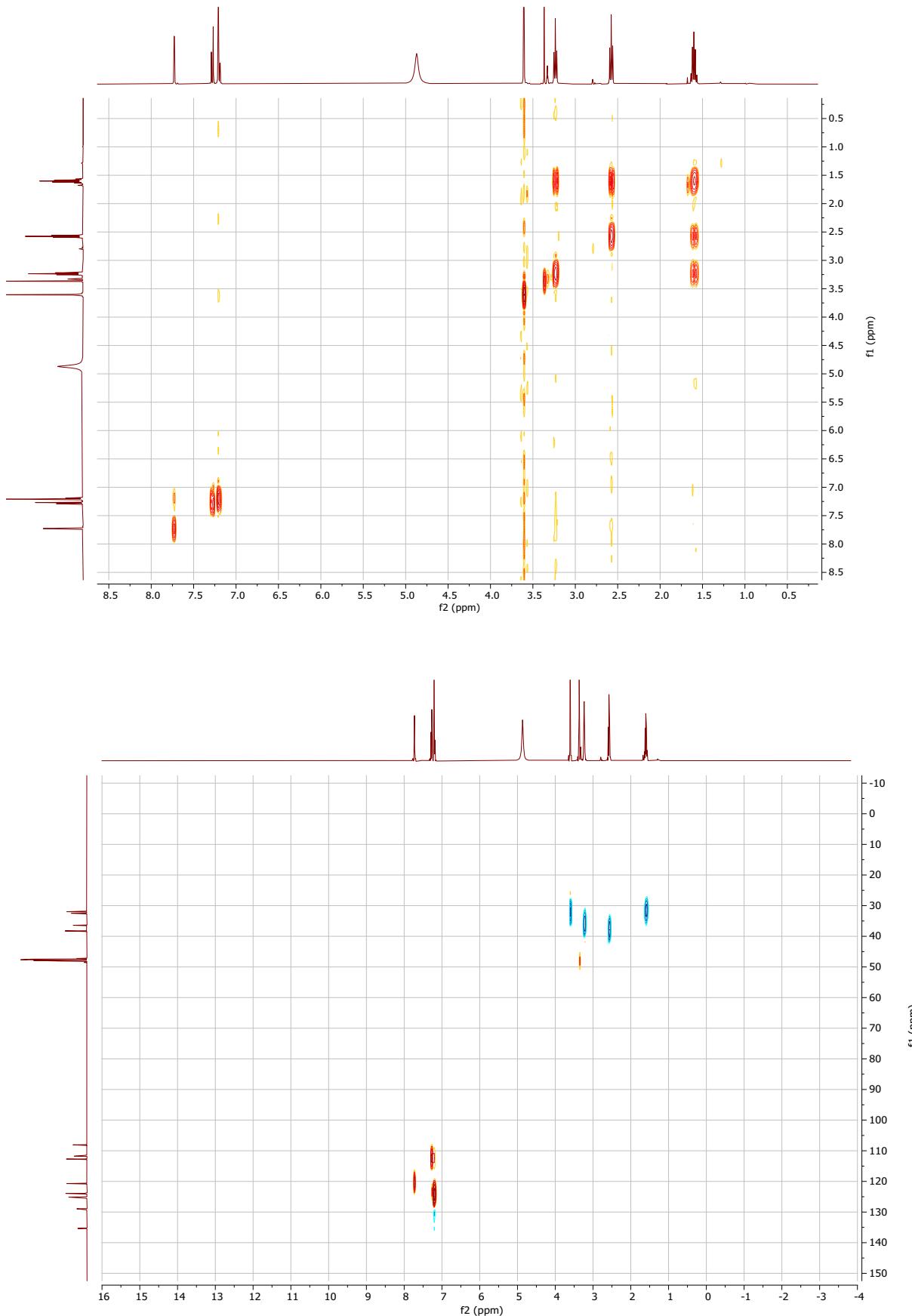


Figure S7. HMBC spectrum of **8a** in Methanol-*d*₄

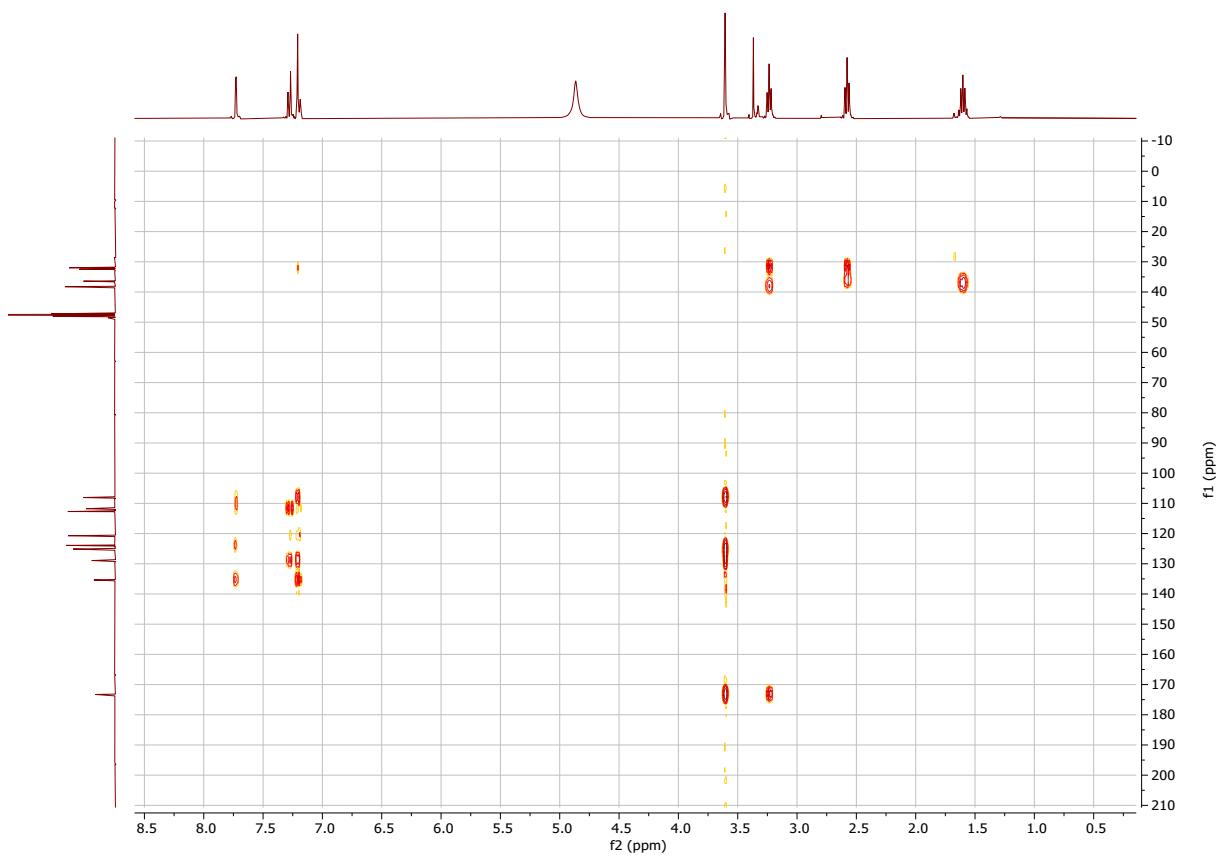


Figure S8. ^1H -NMR and ^{13}C -NMR spectrum of **8b** in Methanol- d_4

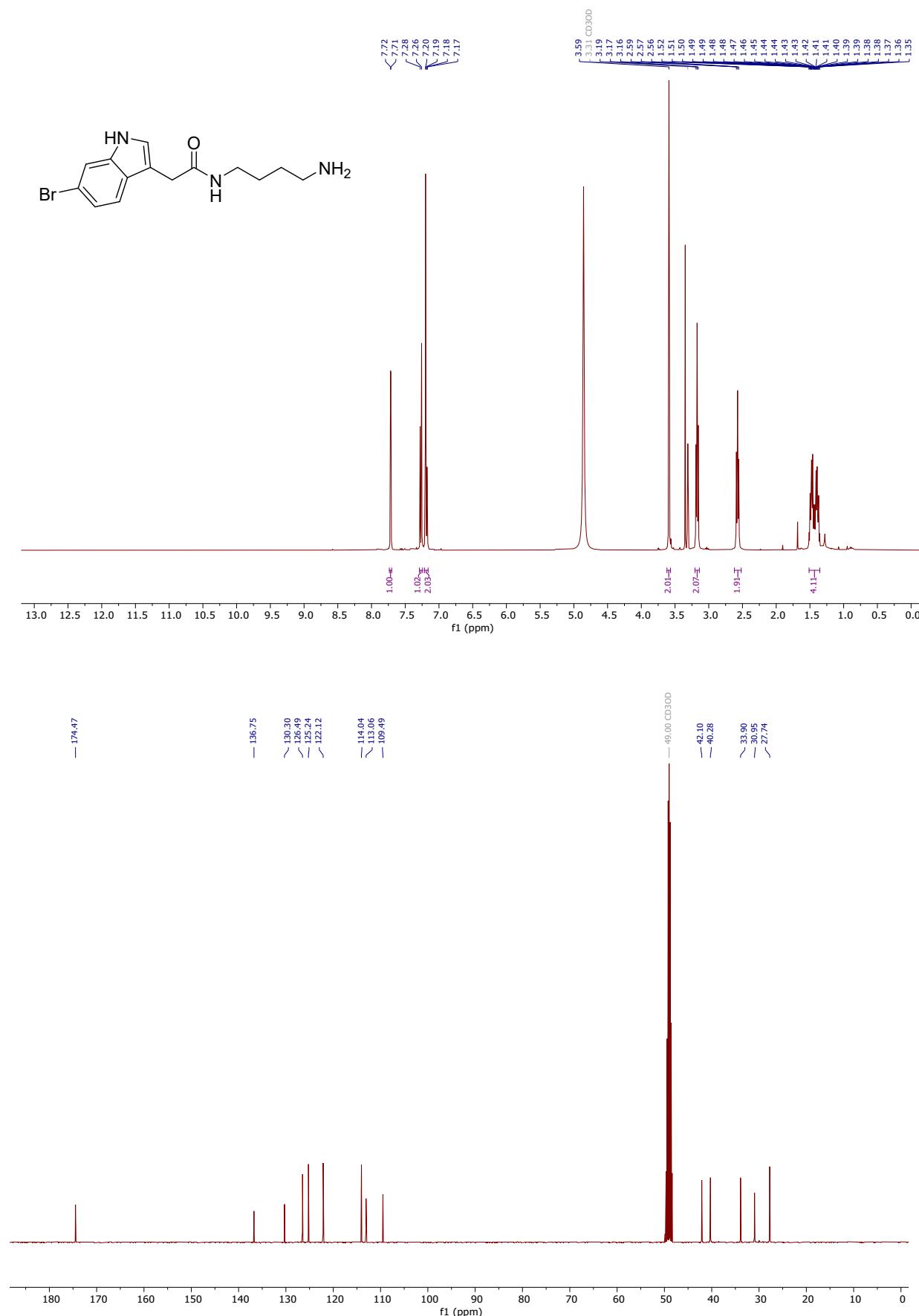


Figure S9. ^1H -NMR and ^{13}C -NMR spectrum of **8c** in Methanol- d_4

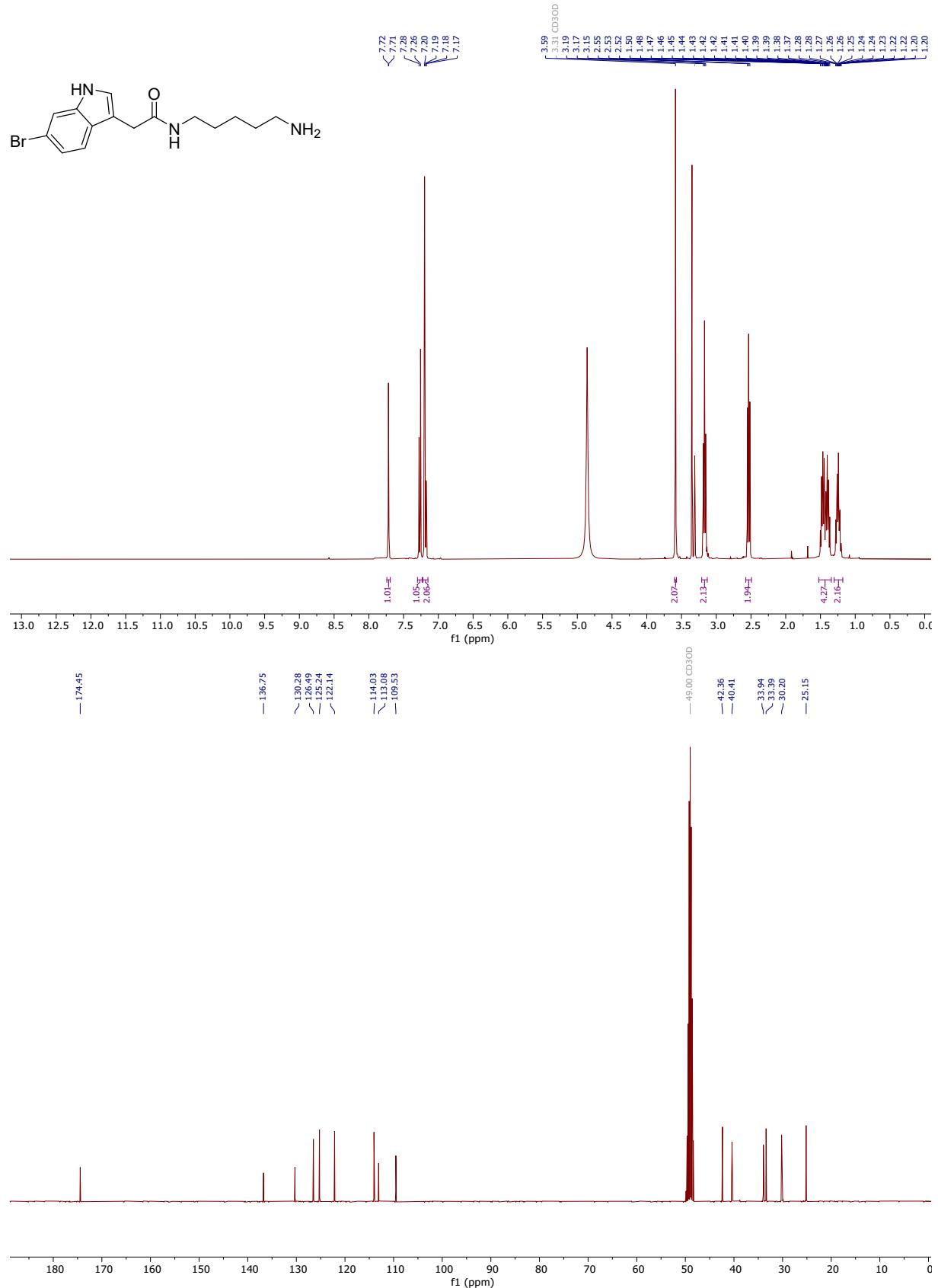


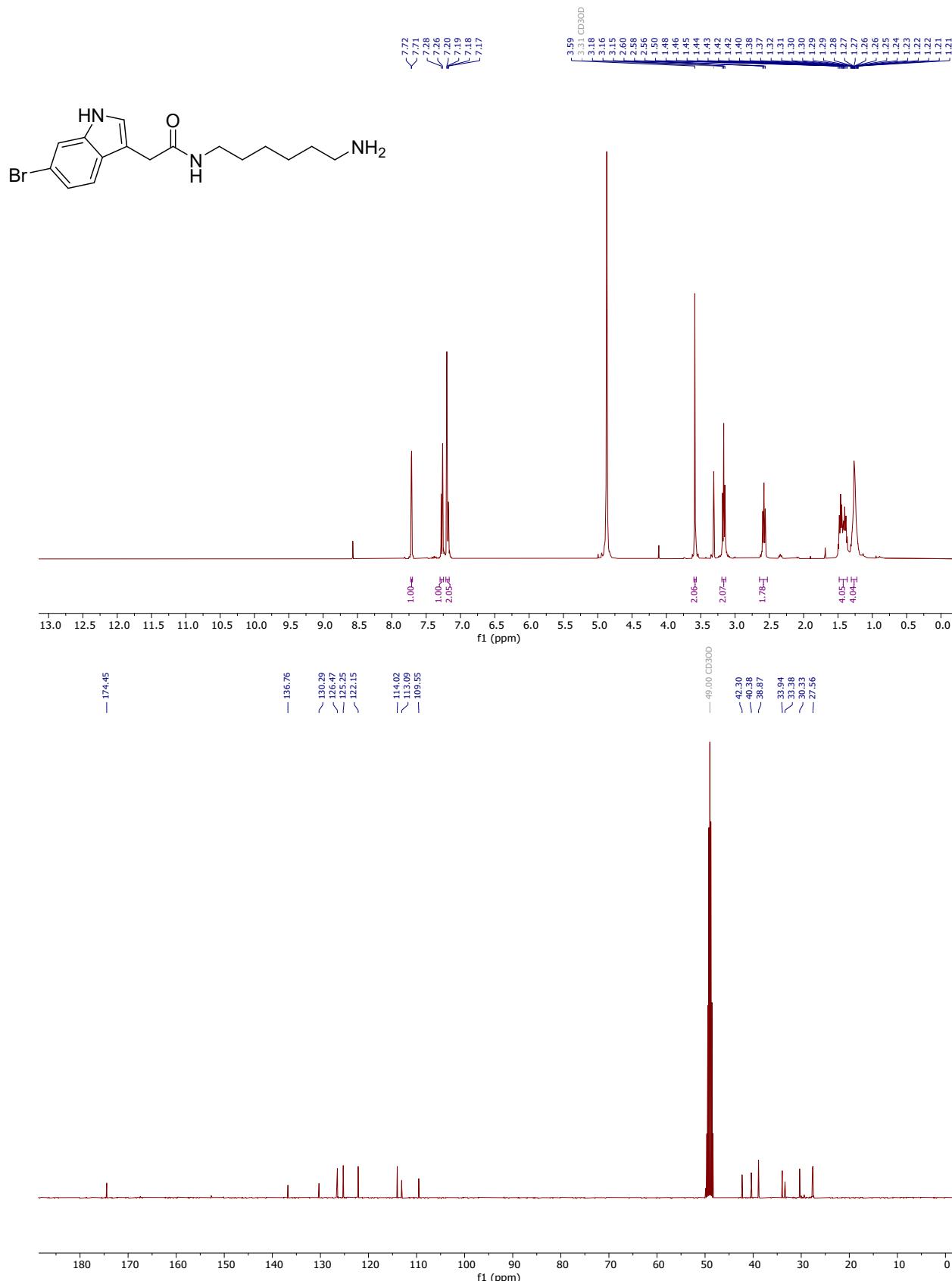
Figure S10. ^1H -NMR and ^{13}C -NMR spectrum of **8d** in Methanol- d_4 

Figure S11 ^1H -NMR and ^{13}C -NMR spectrum of **8e** in Methanol- d_4

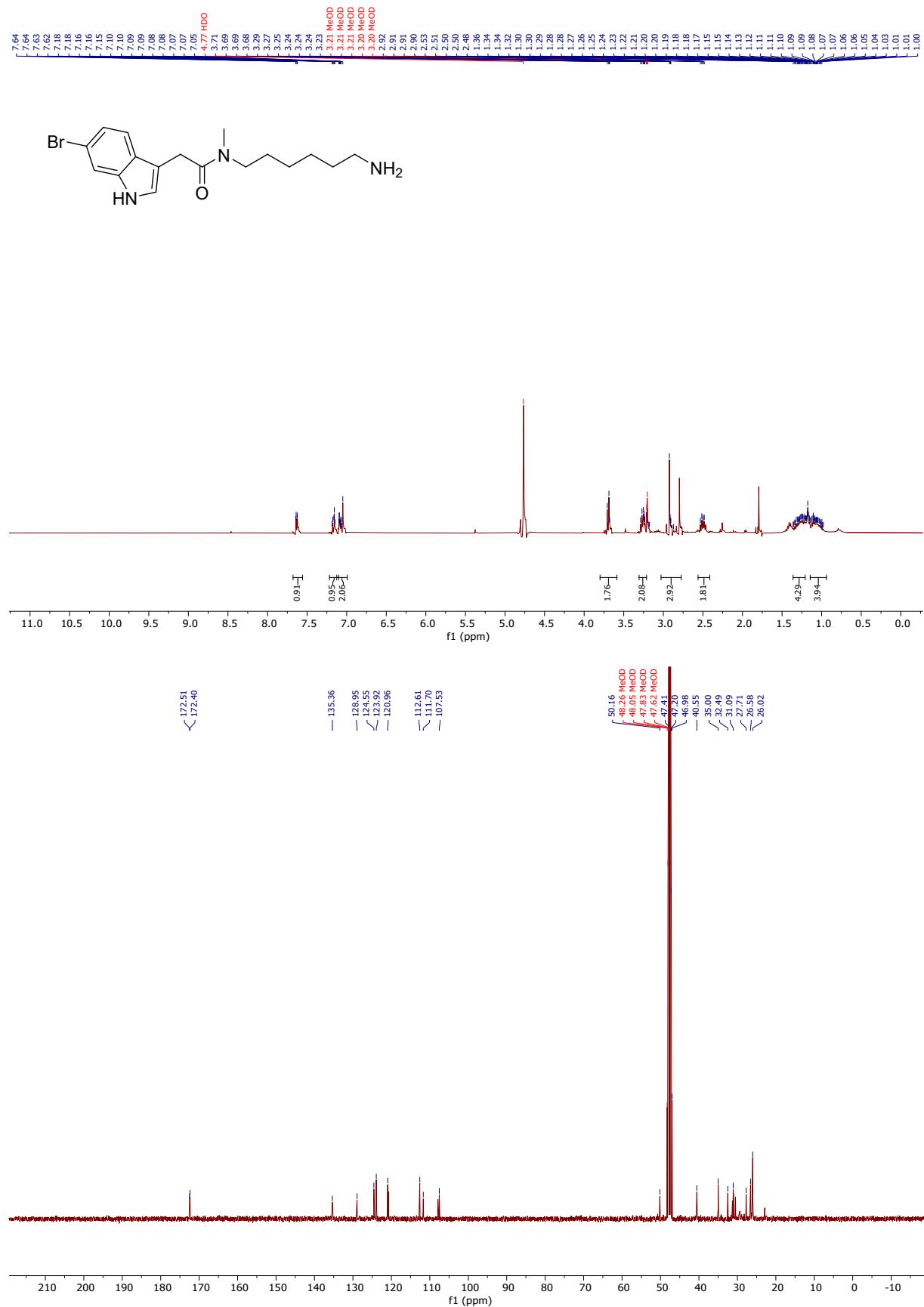


Figure S12. ^1H -NMR and ^{13}C -NMR spectrum of **9a intermediate** in Methanol- d_4

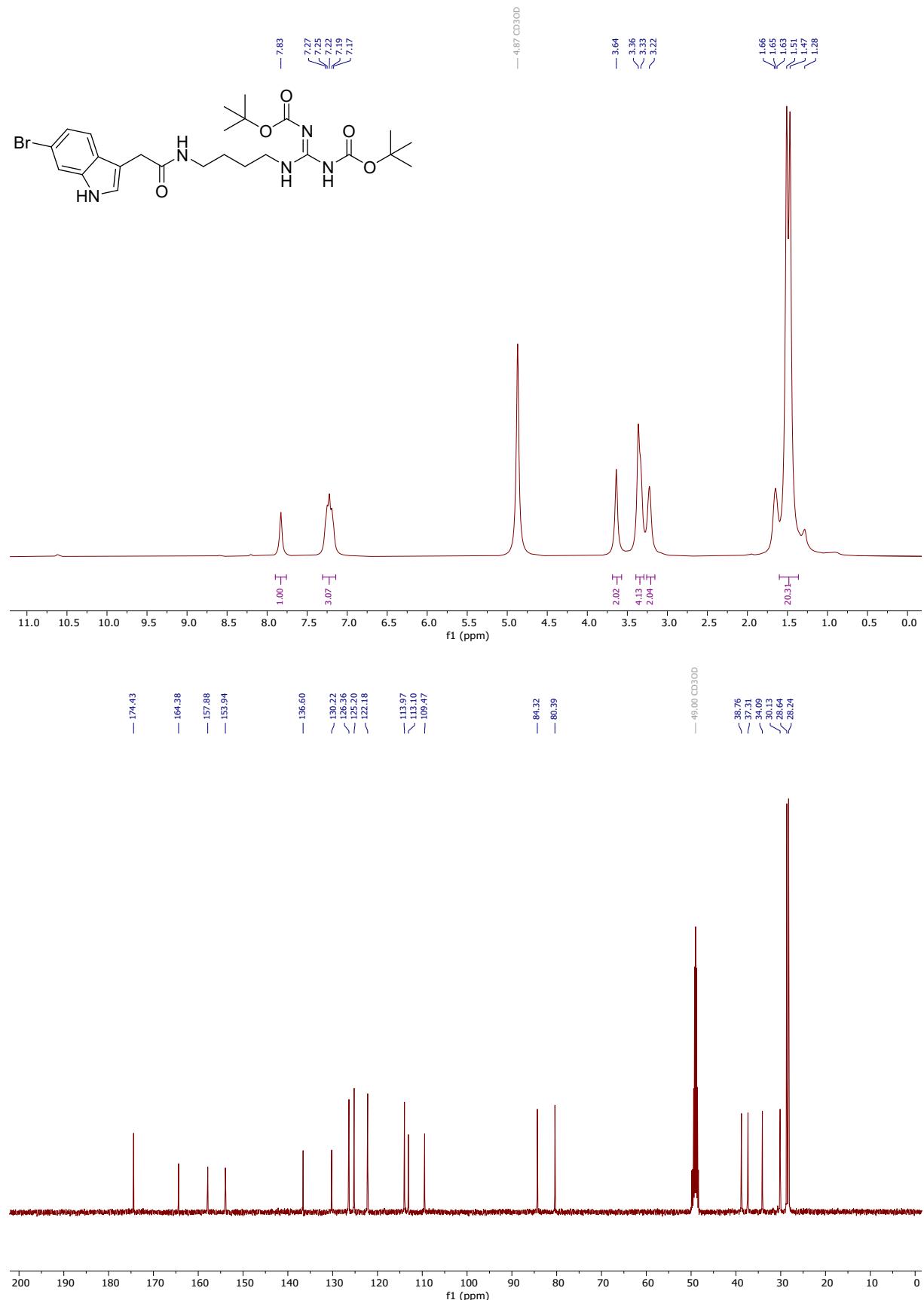


Figure S13. ^1H -NMR and ^{13}C -NMR spectrum of **9a** in Methanol- d_4

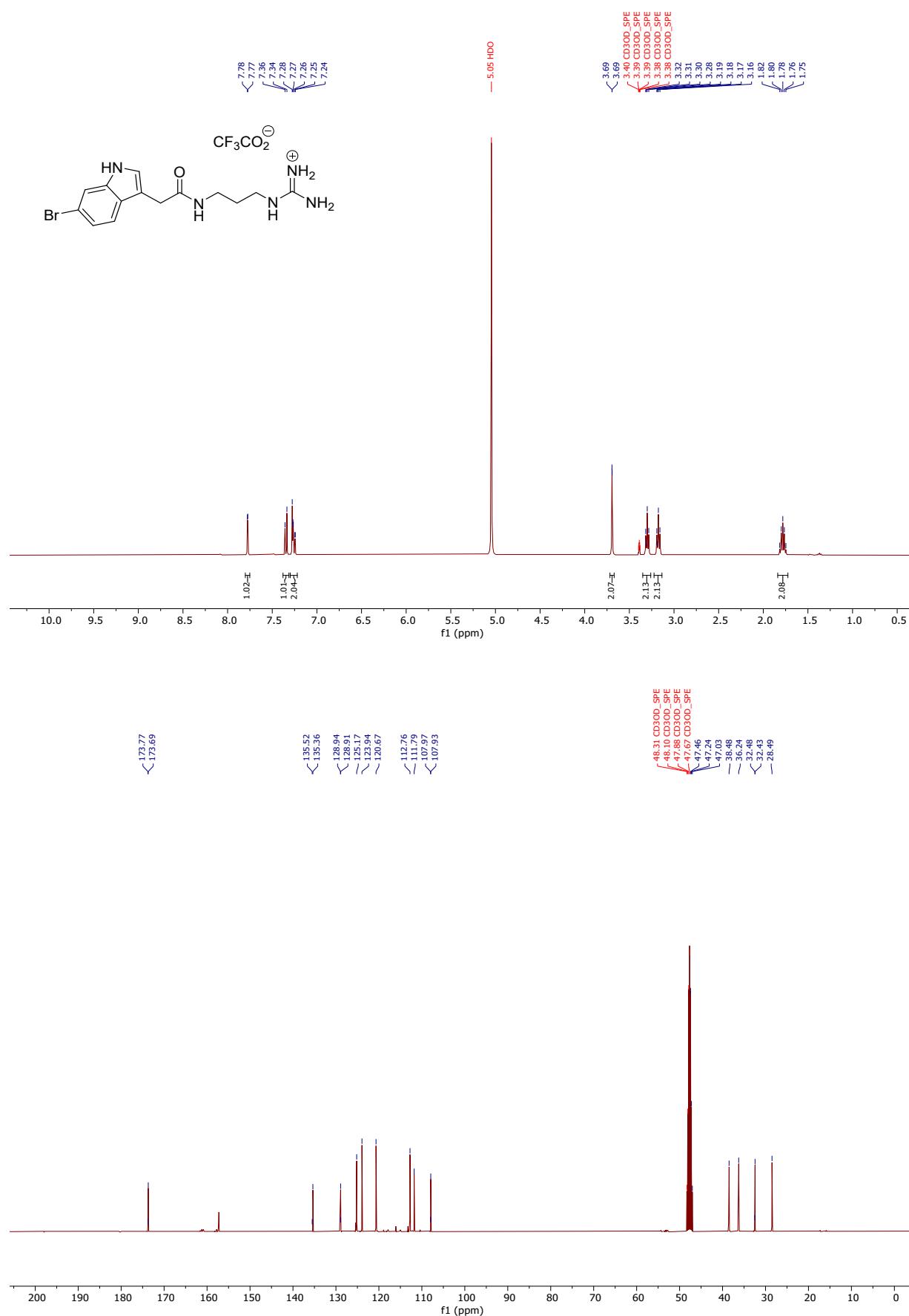


Figure S14. ^1H -NMR and ^{13}C -NMR spectrum of **9b intermediate** in Methanol- d_4

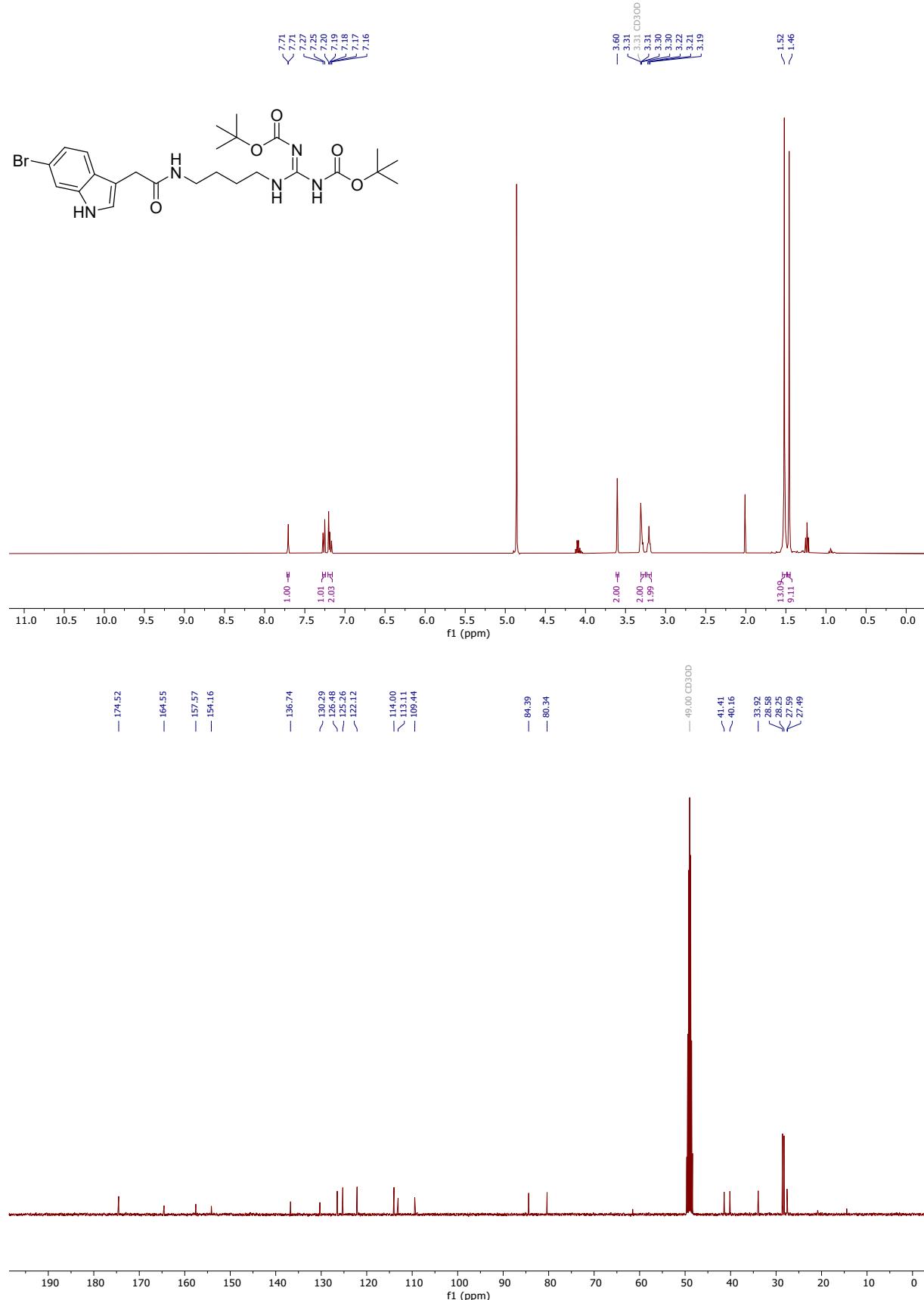


Figure S15. ^1H -NMR and ^{13}C -NMR spectrum of **9b** in Methanol- d_4

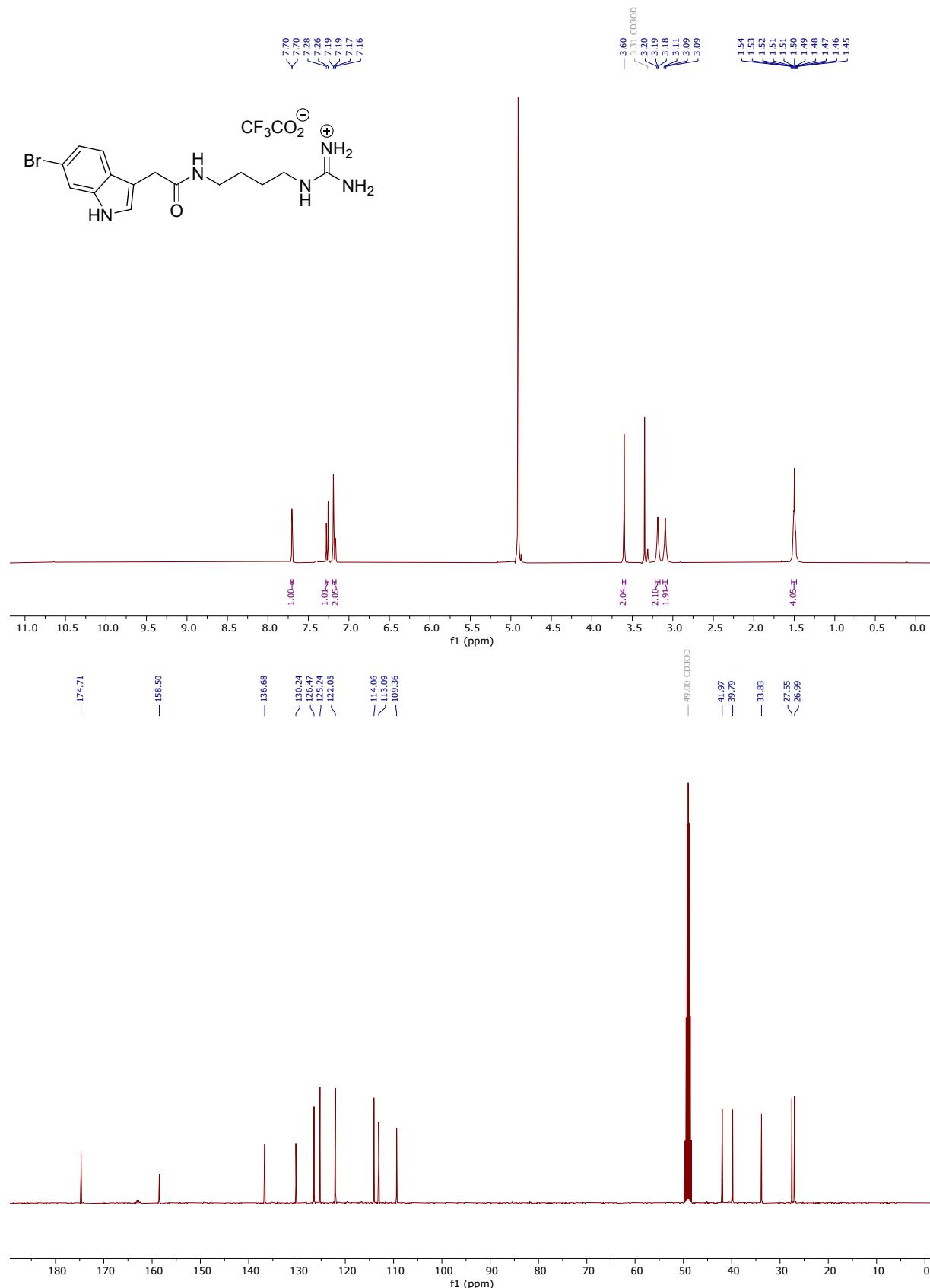


Figure S16. ^1H -NMR and ^{13}C -NMR spectrum of **9c intermediate** in Methanol- d_4

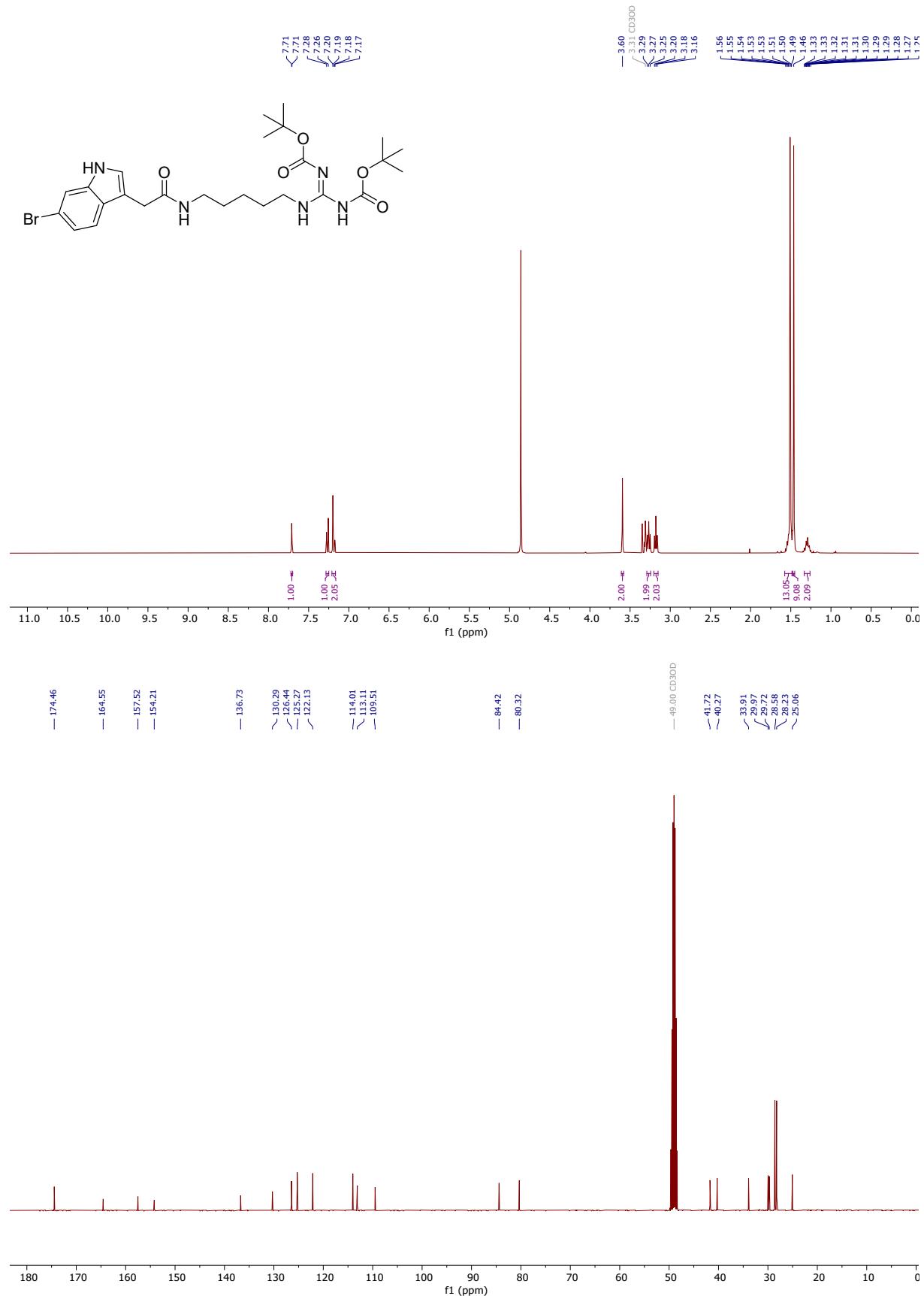


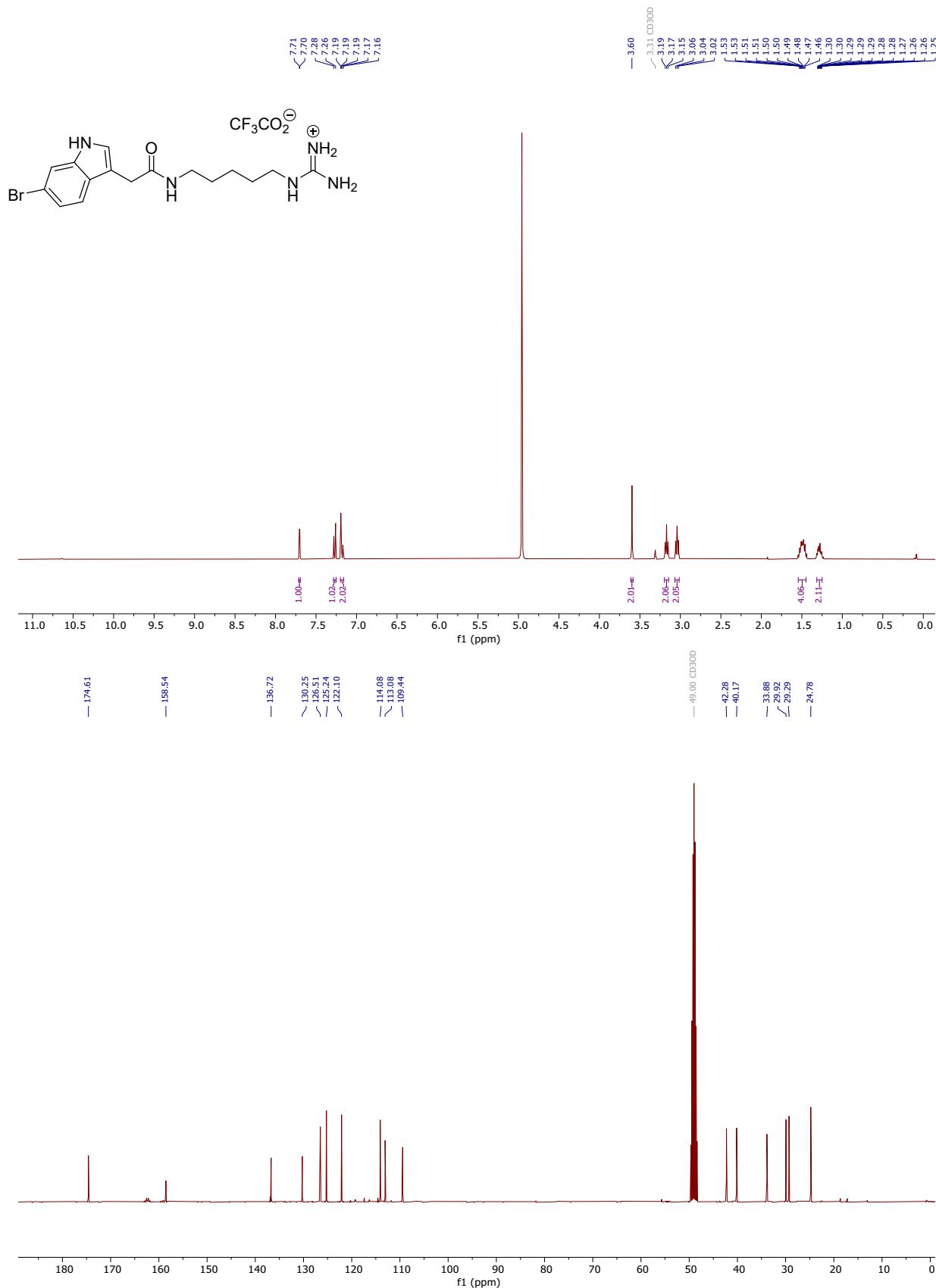
Figure S17. ^1H -NMR and ^{13}C -NMR spectrum of **9c** in Methanol- d_4 

Figure S18. COSY and HSQC spectrum of **9c** in Methanol-*d*₄

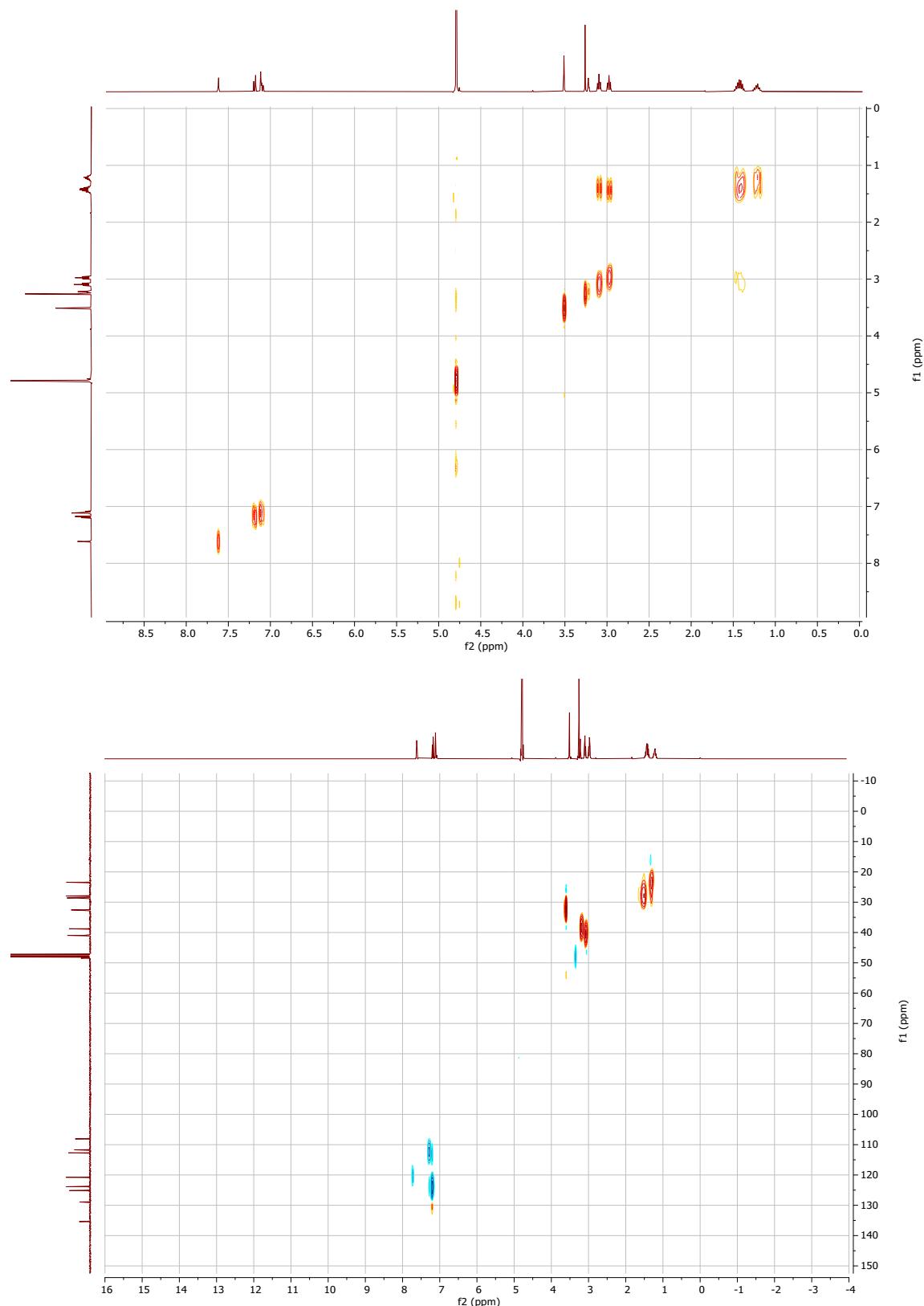


Figure S19. HMBC spectrum of **9c** in Methanol-*d*₄

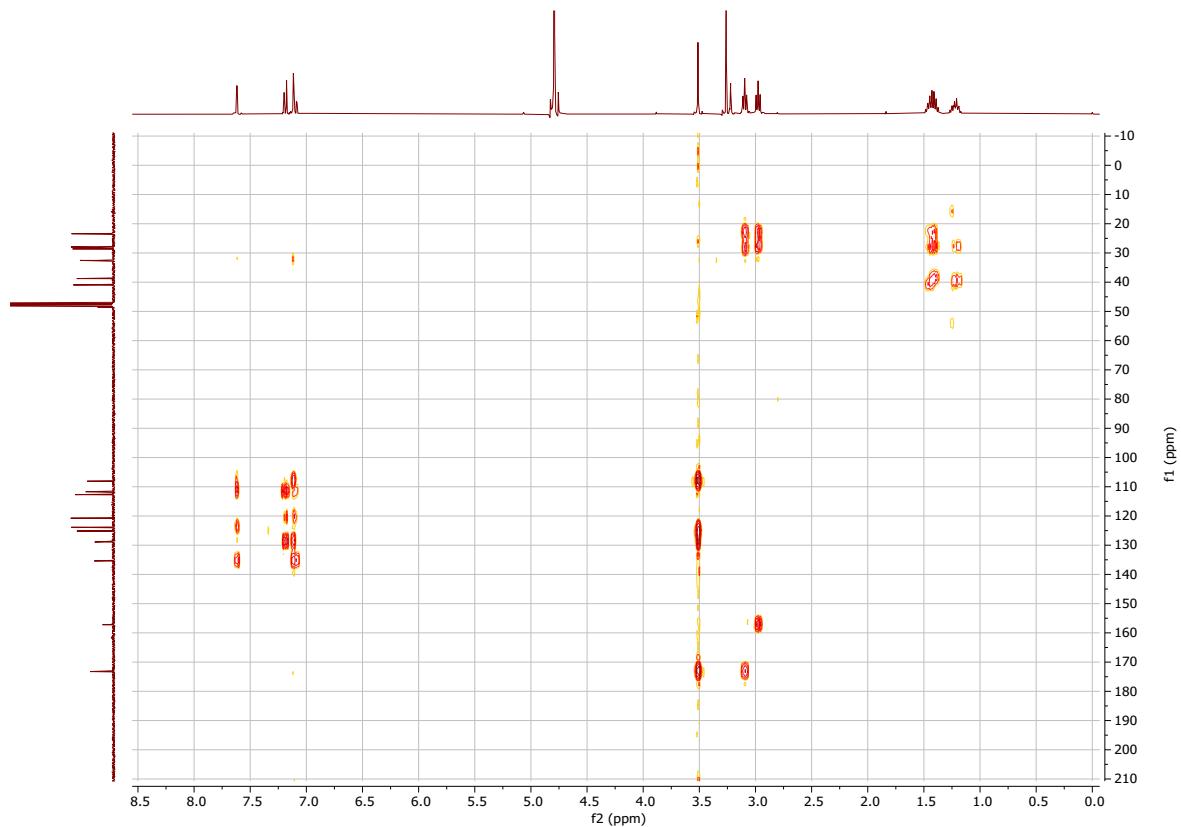


Figure S20. ^1H -NMR spectrum of **9d intermediate** in Methanol- d_4

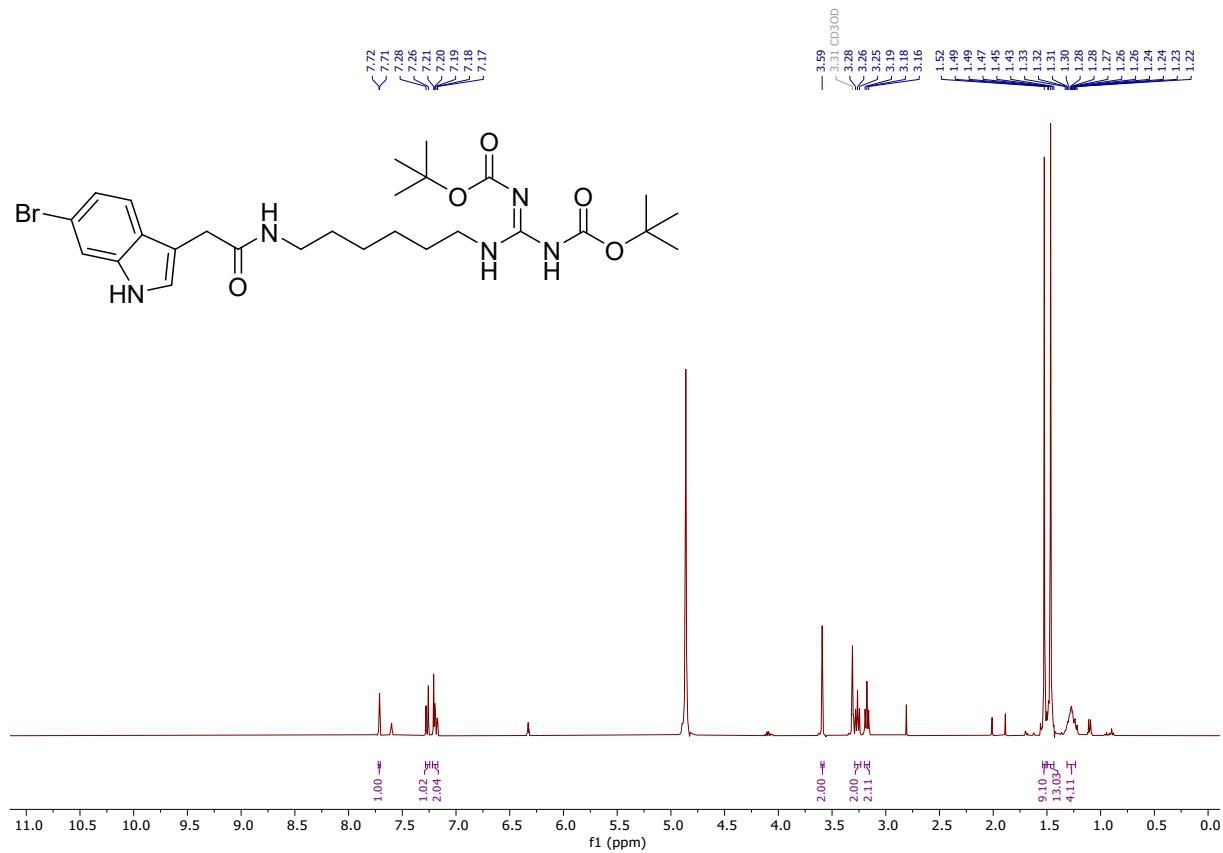


Figure S21. ^1H -NMR and ^{13}C -NMR spectrum of **9d** in Methanol- d_4

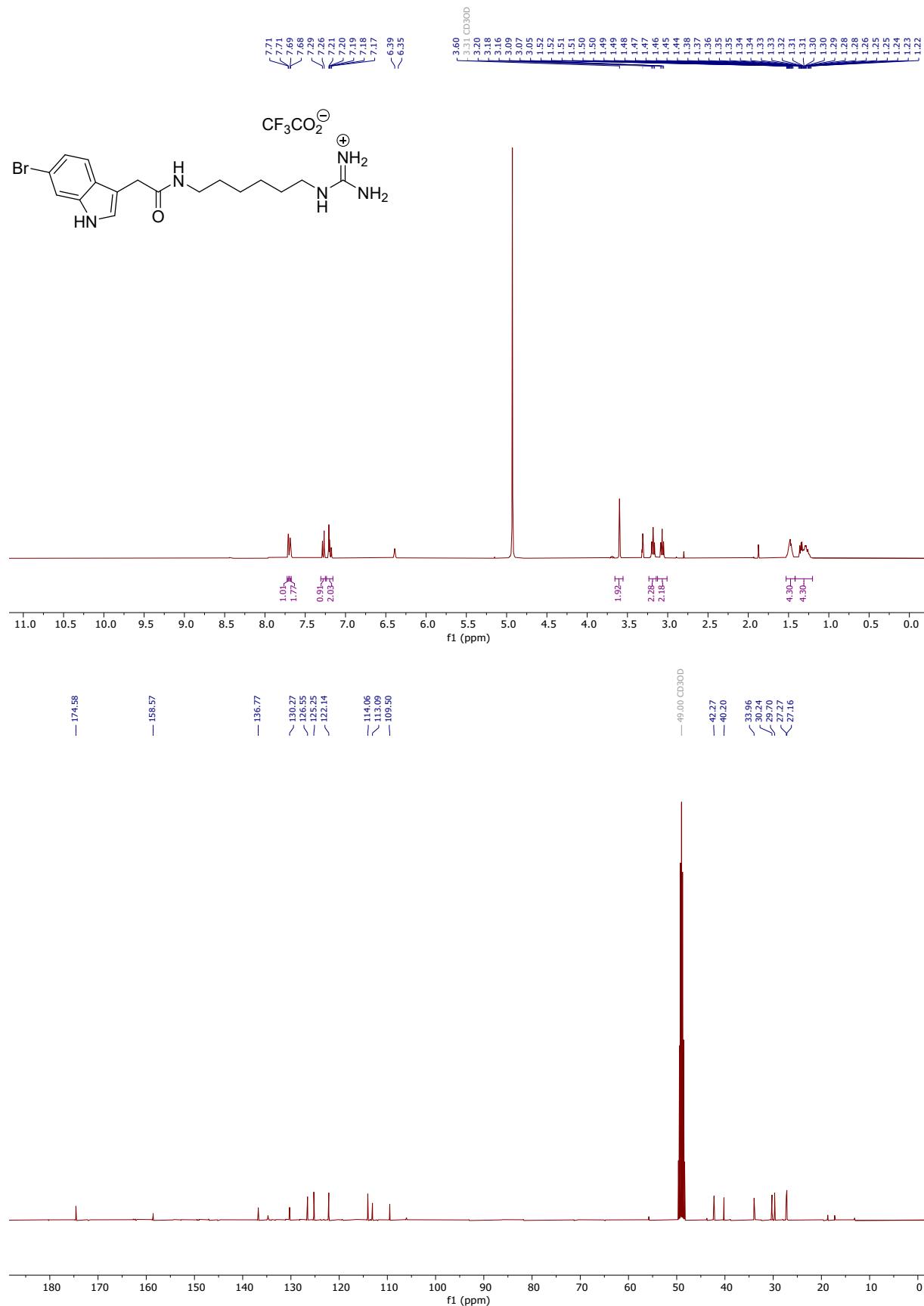


Figure S22. ^1H -NMR and ^{13}C -NMR spectrum of **9e** in Methanol- d_4

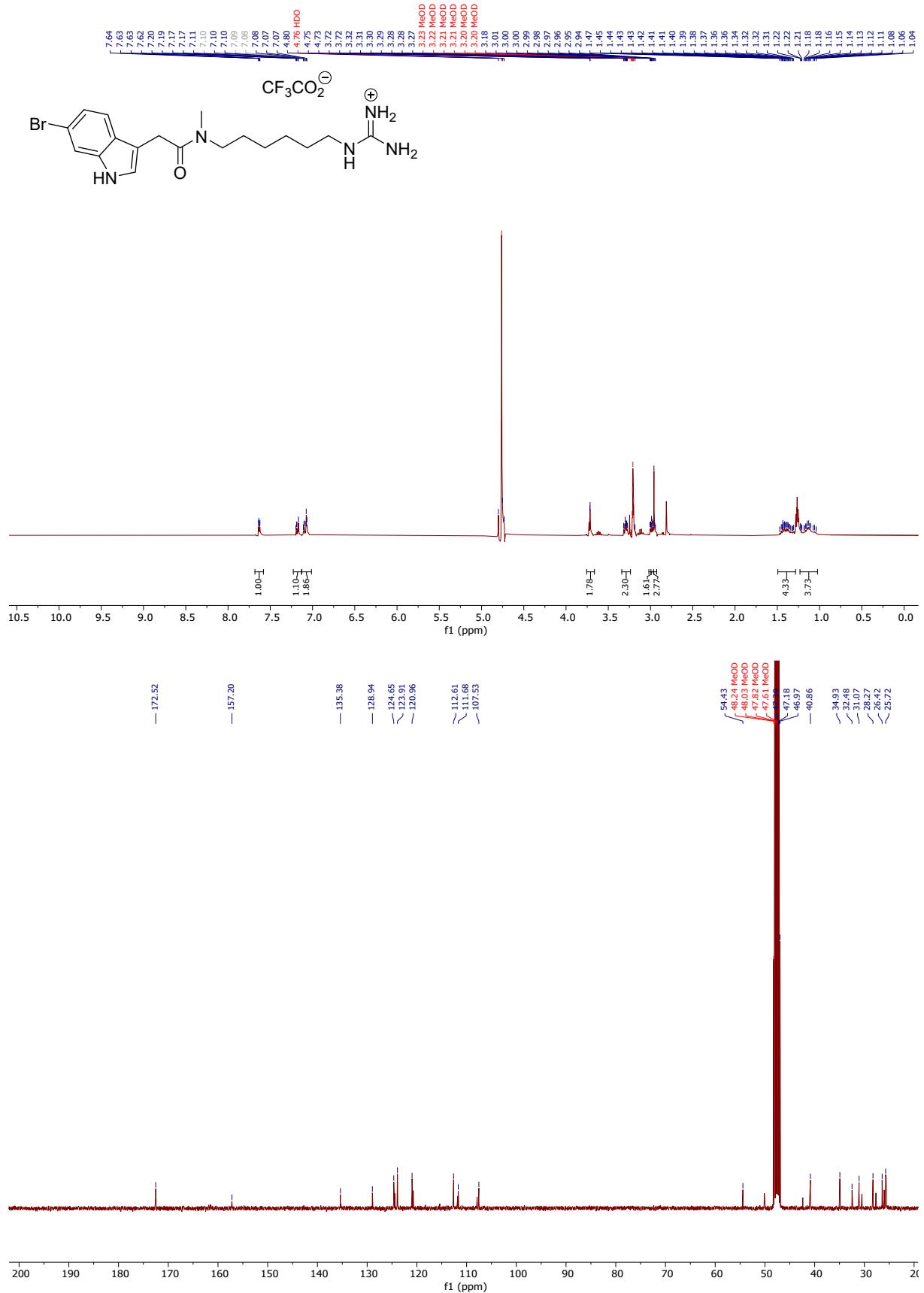


Figure S23. ^1H -NMR and ^{13}C -NMR spectrum of **10a** in Methanol- d_4

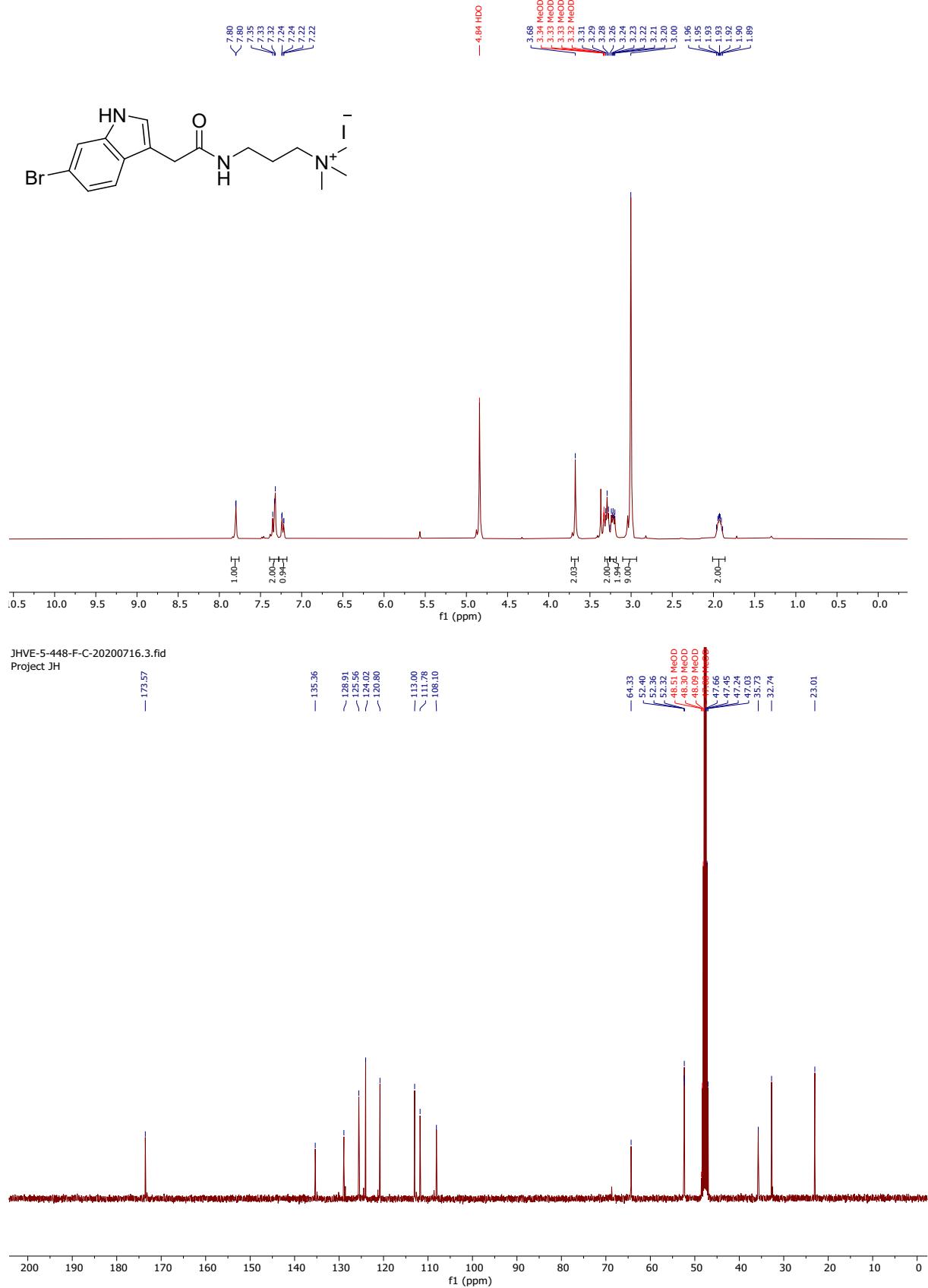


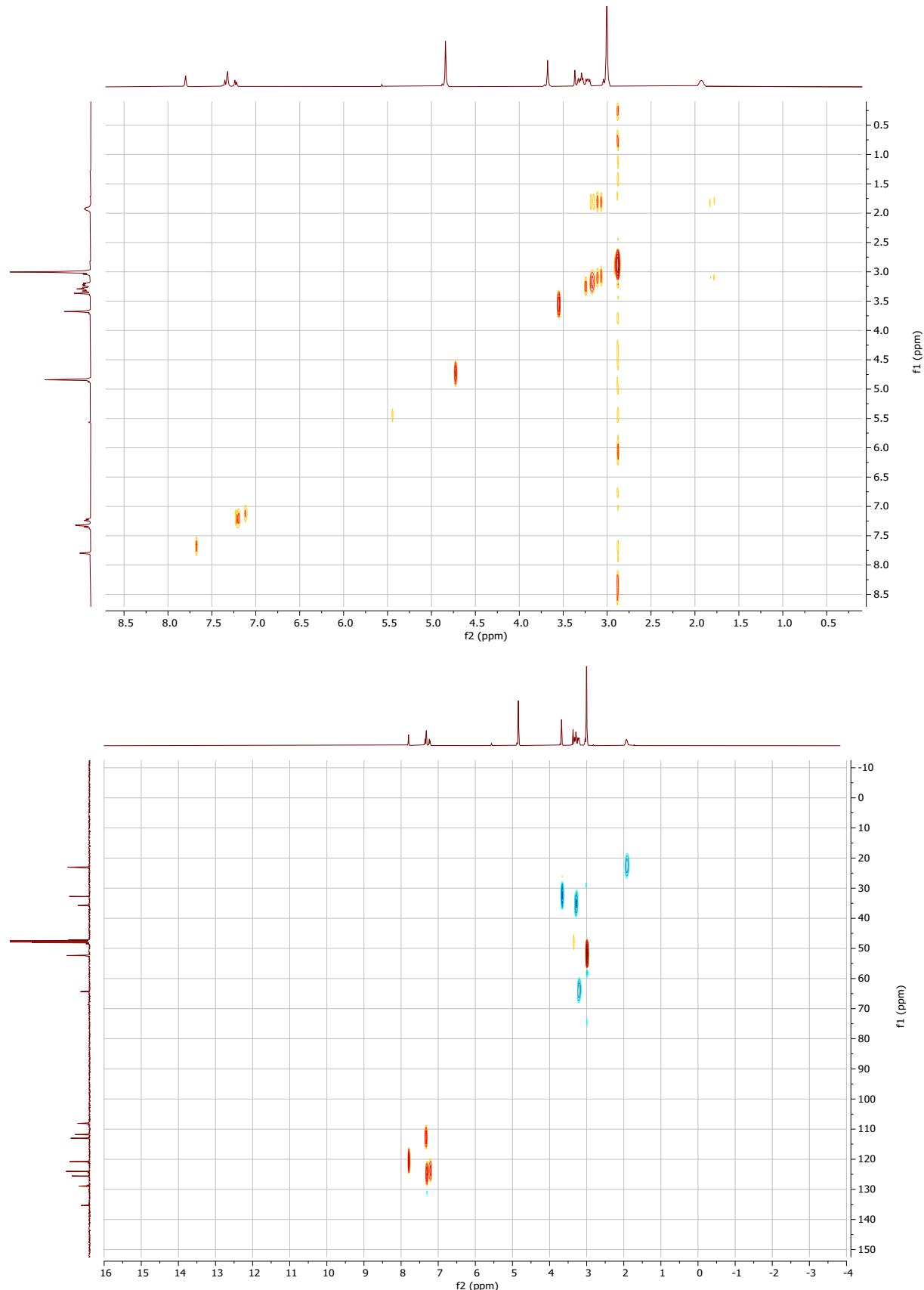
Figure S24. COSY and HSQC spectrum of **10a** in Methanol-*d*₄

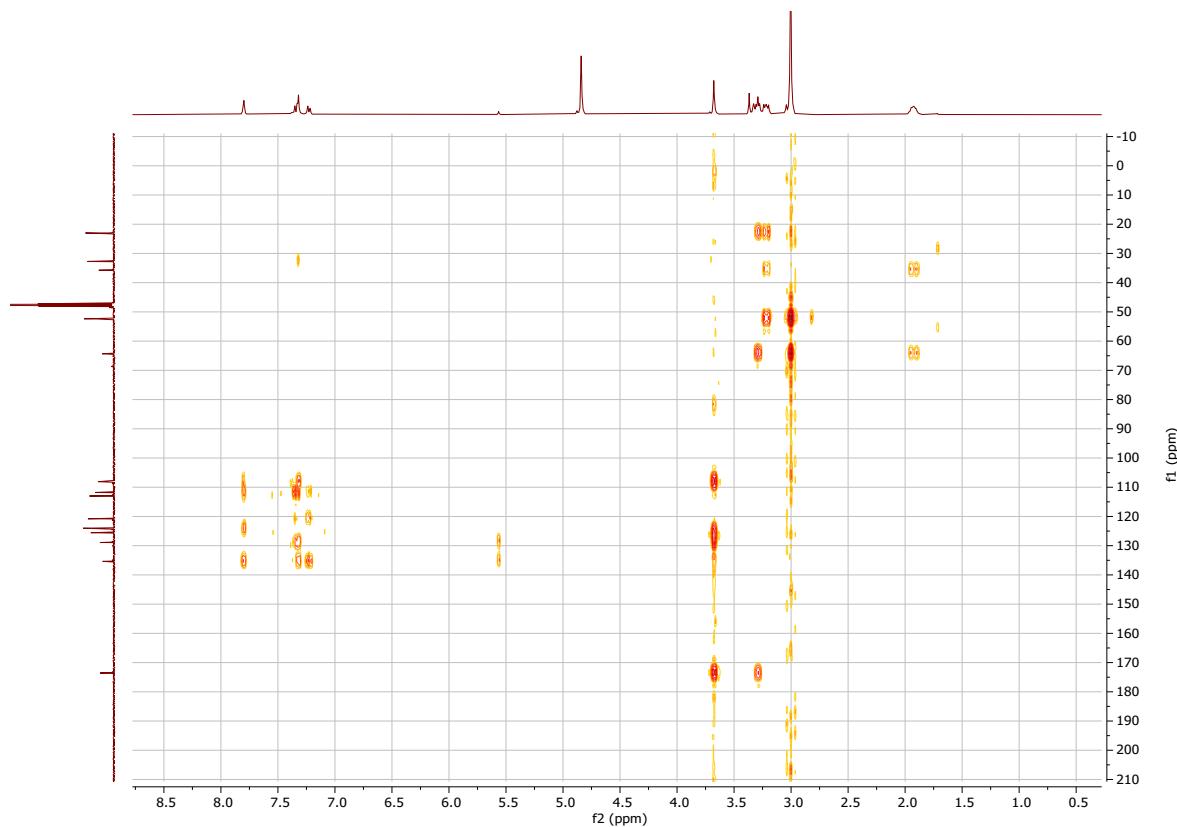
Figure S25. HMBC spectrum of **10a** in Methanol-*d*₄

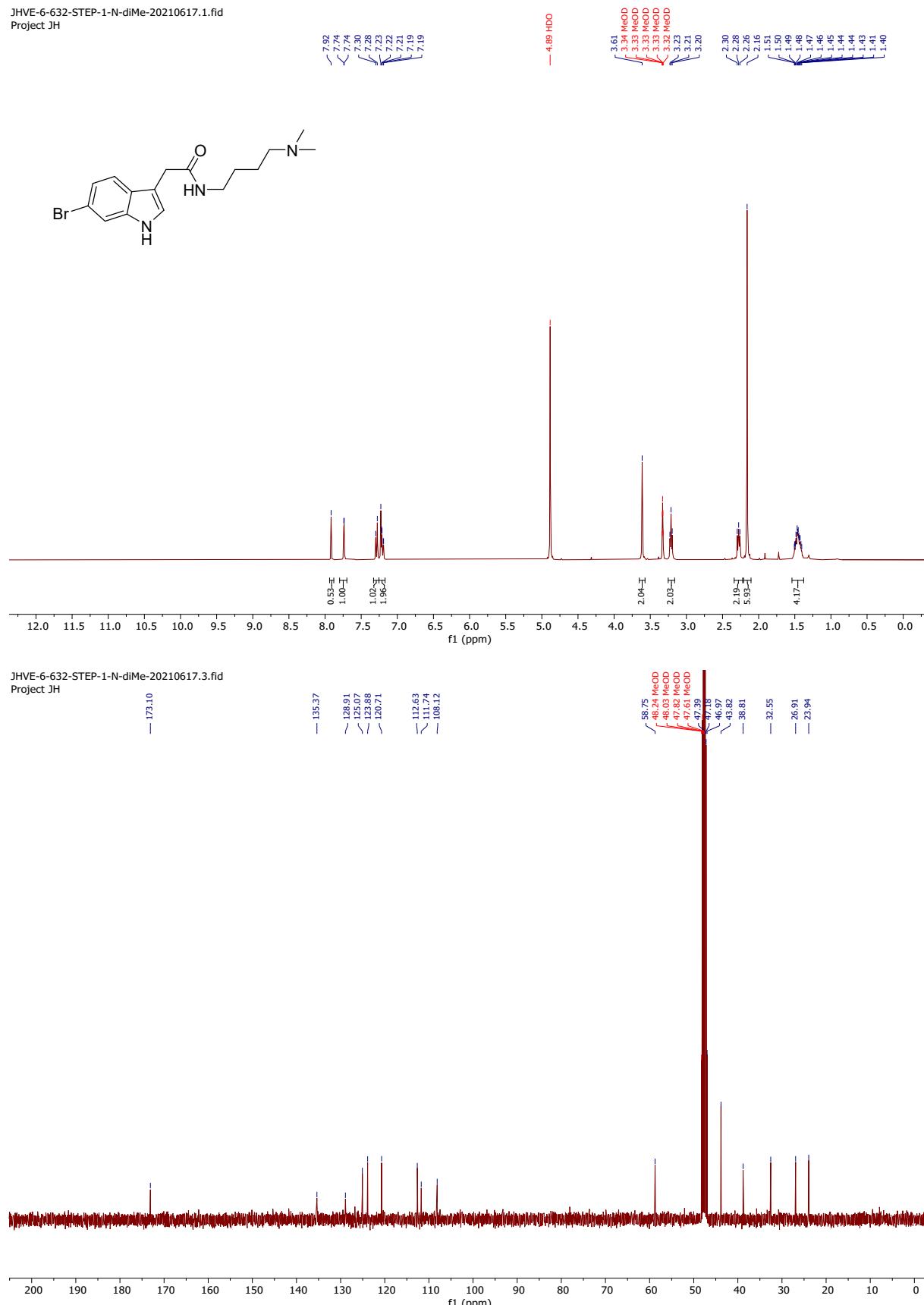
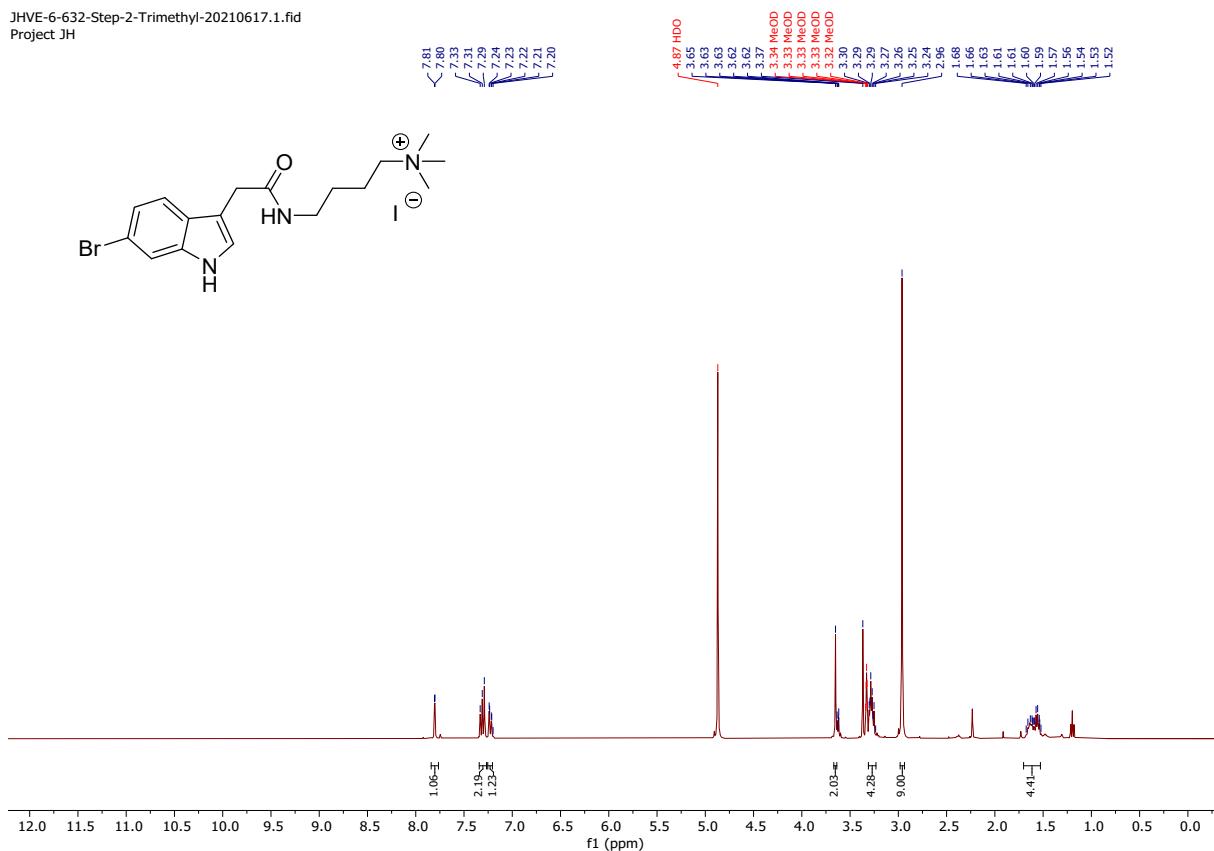
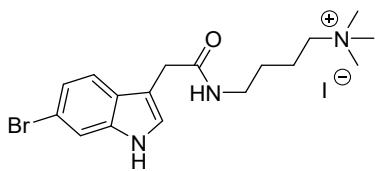
Figure S26. ^1H -NMR and ^{13}C -NMR spectrum of **10b intermediate** in Methanol- d_4 

Figure S27. ^1H -NMR and ^{13}C -NMR spectrum of **10b** in Methanol- d_4

JHVE-6-632-Step-2-Trimethyl-20210617.1.fid
Project JH



JHVE-6-632-Step-2-Trimethyl-20210617.3.fid
Project JH

Figure S28. ^1H -NMR and ^{13}C -NMR spectrum of **10c intermediate** in Methanol- d_4

JHVE-6-633-Step-1-N-DiMe-20210617.1.fid
Project JH

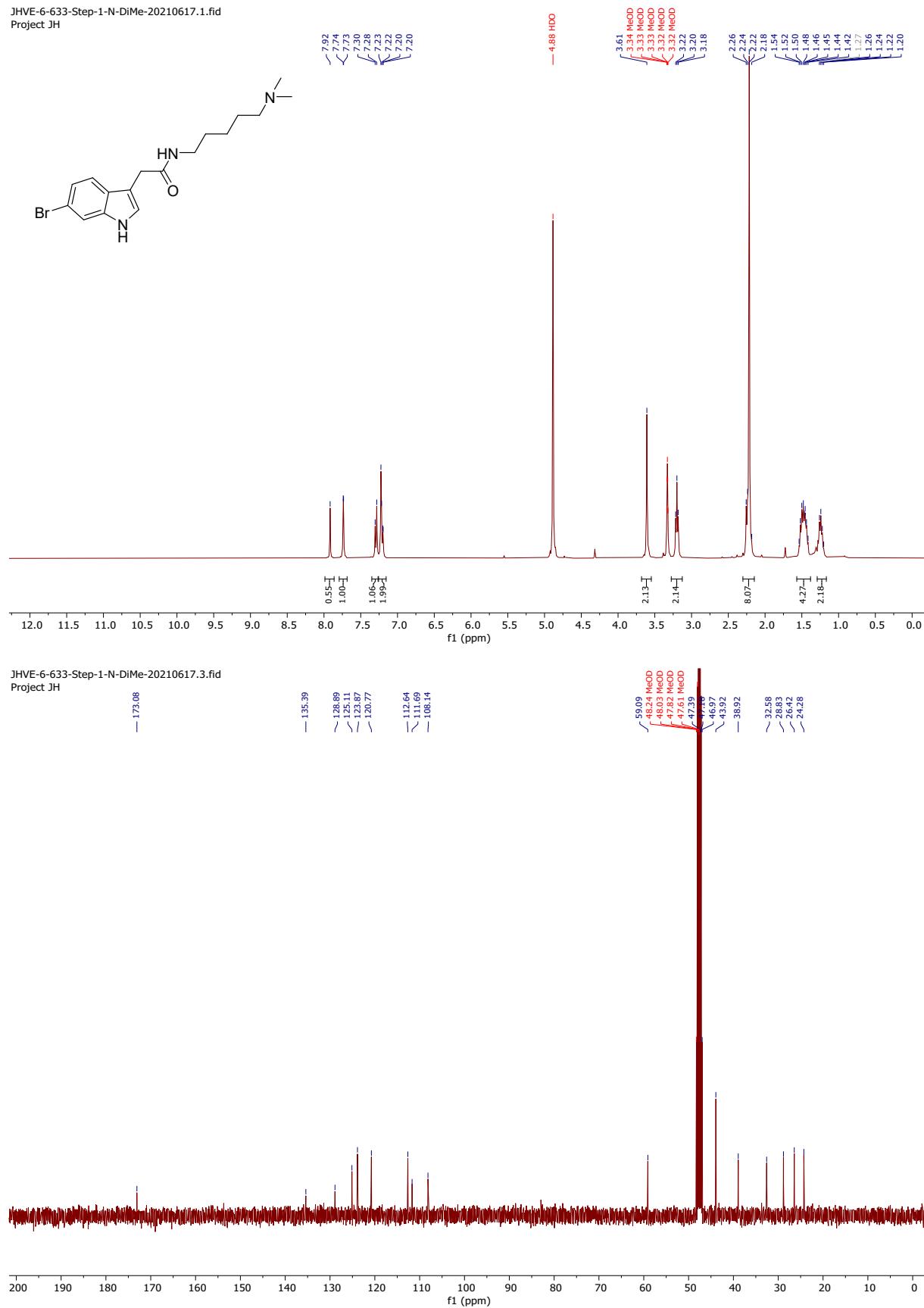
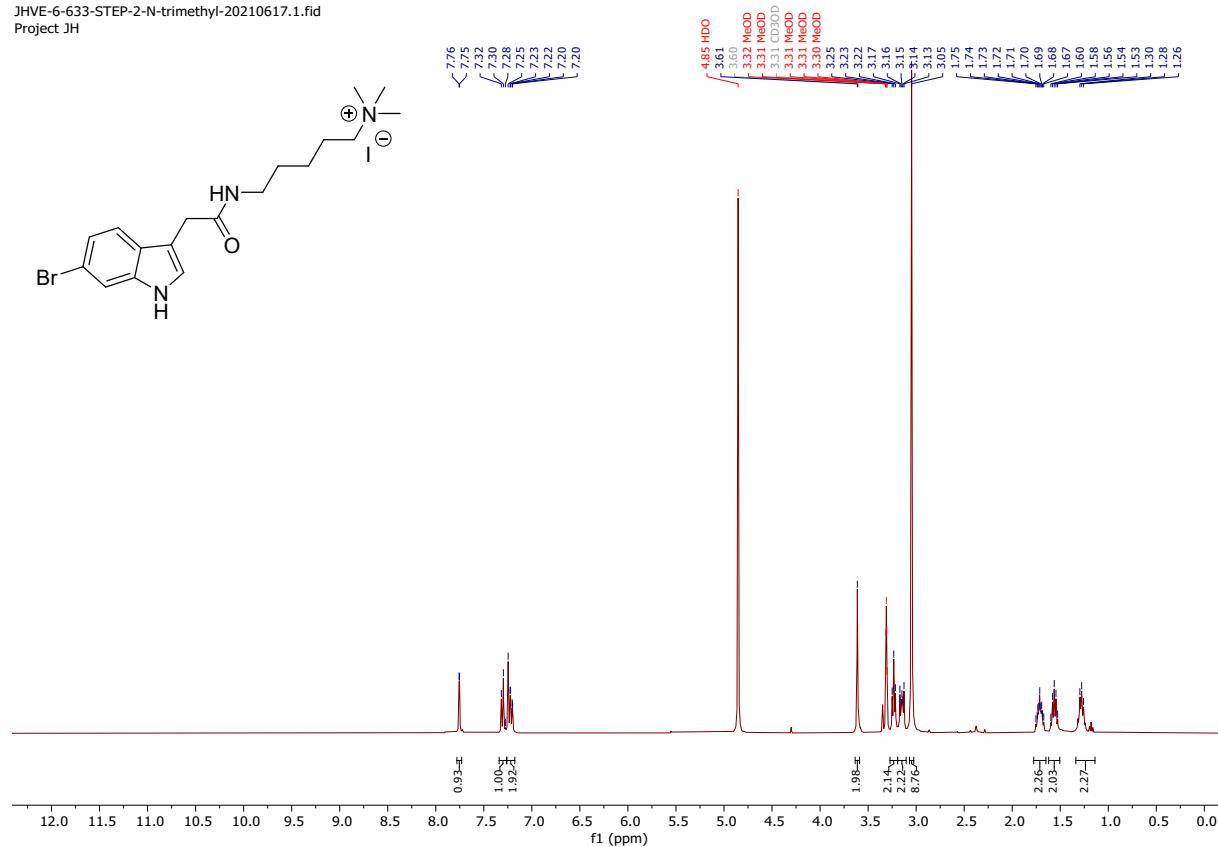
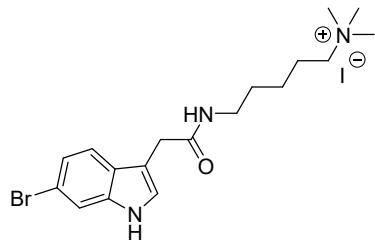


Figure S29. ^1H -NMR and ^{13}C -NMR spectrum of **10c** in Methanol- d_4

JHVE-6-633-STEP-2-N-trimethyl-20210617.1.fid
Project JH



JHVE-6-633-STEP-2-N-trimethyl-20210617.8.fid
Project JH

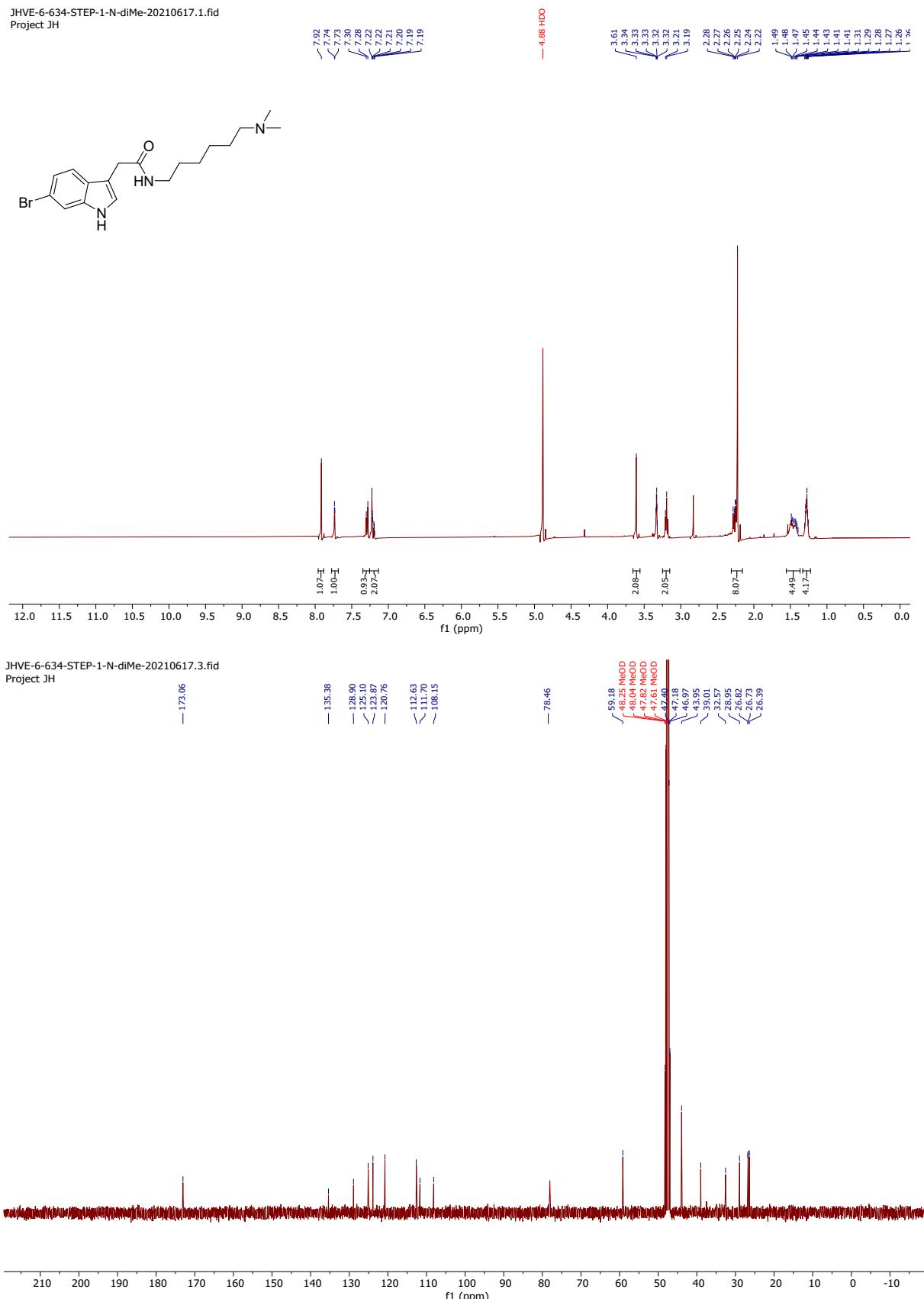
Figure S30. ^1H -NMR and ^{13}C -NMR spectrum of **10d intermediate** in Methanol- d_4 

Figure S31. ^1H -NMR and ^{13}C -NMR spectrum of **10d** in Methanol- d_4

